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DERMATOLOGISTS FOR THE ARMY AND NAVY

WILLIAM H. GUY, M.D.

PITTSBURGH

In this communication I propose to answer some questions bearing on the subject of dermatologists for the armed forces of the United States during the present emergency. It is important to know: that dermatosyphilologists are needed; how many are needed; that well trained men will be utilized in that branch of medicine in which they are proficient; whether it is possible for dermatologists already in the service to be transferred to their specialty, and, finally, what course dermatologists are to pursue in applying for commissions to obtain such assignments. That there has been some dissatisfaction because of assignments for which men are not qualified is not surprising when one considers the problem as a whole.

According to a statement in the *Providence Medical News*,[1] the estimated number of specialists required per million men in military service under the Protective Mobilization Plan, as prepared prior to December 8, 1941, was as follows: allergists, 98; anesthetists, 270; anesthetists (intratracheal), 27; cardiologists, 208; dermatologists, 98; gastroenterologists, 196; general operating surgeons, 800; assistants to operating surgeons, 259; internists, 713; laboratory specialists (clinical pathologists, bacteriologists, etc.), 651; neurologists, 196; neuropsychiatrists, 192; neurosurgeons, 134; ophthalmologists, 100; orthopedic surgeons, 459; otorhinolaryngologists, 281; plastic and maxillofacial surgeons, 136; roentgenologists, 348, thoracic surgeons, 125; tuberculosis specialists, 98; urologists and syphilologists, 293.

In Chicago on Feb. 15, 1942 there was a special meeting of the Association of American Medical Colleges, called for the purpose of determining what the medical schools of the country could do to help in the emergency and with especial reference to the adoption of an accelerated program of medical education. The meeting was addressed by Surgeon General McIntire of the Navy, Colonel Lull, representing

Read before the Section on Dermatology and Syphilology at the Ninety-Third Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1942.

1. Drafting the Doctor, editorial, Providence M. News **3**:3 (March) 1942.

the Surgeon General of the Army, Surgeon General Parran of the Public Health Service, Major Seeley, of Procurement and Assignments, and General Hershey, Chief of Selective Service. In the course of the discussion it was stated that during 1942 all physicians under the age of 36 would probably be in the Army if they were physically fit and not engaged in work considered essential to the defense program in their present positions and that during 1943 all physicians up to the age of 45, with the same exceptions, would be in the service. In a letter dated March 10, 1942, addressed to deans of medical schools, Dr. William C. Rappleye, Dean of Columbia University College of Physicians and Surgeons, Chairman of the Committee on Preparedness of the Association of American Medical Colleges and President of the Advisory Board for Medical Specialists, estimated that during the year 1942, for an army of approximately 3,600,000 men, 2,400 additional physicians would be needed and that 294 of these were to be dermatologists. On the basis of these figures alone it would seem advisable that all physicians within this age group take active steps to enter the service as soon as possible.

In order to obtain more specific information in answer to the questions I have propounded, letters were dispatched to the Surgeons General of the Army, Navy and Public Health Service and to the Procurement and Assignment Bureau.

The following reply was received from Col. George F. Lull, Assistant in the Office of the Surgeon General of the United States Army:

This will acknowledge your letter of April 17, relative to the utilization of dermatologists in the Army.

As you know, it is very difficult to assign all specialists to positions where they will do the work they are accustomed to doing in civil life. When a line officer enters the Army, he gives up his civil occupation entirely and has to learn a new one, so many medical officers entering the Army have to adjust themselves to their surroundings and learn new occupations.

I shall attempt to answer your questions, but these answers will, of course, depend on so many things that it will be impossible to be definite on all of them.

1. Are dermatologists needed? If so, how many? Answer: Dermatologists are needed in the Army. The exact number is not known. They can be utilized at our larger hospitals, but as a rule there is not sufficient work to employ them exclusively in dermatology.

2. Can we assure those who volunteer that they will be assigned to dermatology and syphilis? Answer: No. We will try, as far as possible, to assign them to hospitals where they will be employed in the treatment of skin diseases and syphilis. In many places, however, skin cases are treated in a different department from syphilis.

3. Is is possible that those already in the service may be transferred to the line of work in which they are most proficient? Answer: It may be possible to transfer most of these individuals if some one will submit their names to this office.

4. What course is to be pursued by dermatologists applying for commissions to obtain such assignments? Answer: They should state on their applications that they desire such assignments and every attempt will be made to grant their requests. However, that cannot be guaranteed.

The following letter came from Rear Adm. Ross T. McIntire, Surgeon General of the United States Navy:

In reply to your letter of April 7, you are advised all of the Reserve medical officers on active duty who are qualified in dermatology and syphilology are assigned to duty in that specialty with the exception of one medical officer who has requested assignment to duty not involving the specialty for which he is qualified.

At the present time there are twenty-five medical officers of the Naval Reserve on active duty who are qualified in dermatology and syphilology. It is estimated that an additional seventy-five of these specialists will be required within the next year.

While no assurance can be given an applicant for appointment in the Medical Corps of the Naval Reserve that his services will be utilized exclusively in his specialty, every effort is made to assign medical officers to billets where their specialties may be utilized to the best advantage of the Medical Department. In time of war and in a service emergency, it is anticipated it may be necessary to utilize specialists temporarily in assignments other than in their specialties. If this is necessary, it is the policy of this Bureau to return these officers to duty in their specialties as soon as the emergency has been met.

In the event the required number of doctors qualified in dermatology and syphilology do not apply for appointment in the Medical Corps of the Naval Reserve, it is planned to train medical officers in this specialty.

Applicants who desire to apply for appointments in the Medical Corps of the United States Naval Reserve should communicate with the Director of Naval Officer Procurement in the location nearest their place of residence. For your information, there is attached herewith a list of the addresses of the Offices of Naval Officer Procurement now established.

The addresses of the offices of Naval Officer Procurement of the United States Naval Reserve, as of March 18, 1942, are as follows:

First Naval District—150 Causeway Street, Boston

Third Naval District—33 Pine Street, New York

Fourth Naval District—Widener Building, Philadelphia

Fifth Naval District—Chevrolet Parts Building, Norfold and Altamont Streets, Richmond, Va.

Sixth Naval District—Navy Yard, Charleston, S. C.

Seventh Naval District—Langford Building, 121 South-East First Street, Miami, Fla.

Eighth Naval District—New Federal Building, New Orleans, La.

Ninth Naval District—Board of Trade Building, Chicago

Eleventh Naval District—850 Lilac Terrace, Los Angeles

Twelfth Naval District—Central Tower Building, 703 Market Street, San Francisco

Thirteenth Naval District—117 Marion Street, Seattle

Washington, D. C.—1320 "C" Street, North West; telephone, EXecutive 3510

The following communication was received from Dr. Thomas Parran, Surgeon General of the United States Public Health Service:

Receipt of your letter of April 27, 1942, about the need for dermatologists by the Public Health Service, is acknowledged.

1. The Public Health Service has need at the present time for approximately 50 qualified dermatologists.

2. You can assure those who are appointed that they will be assigned to work in dermatology and syphilology.

3. Dermatologists and syphilologists already in the service are for the most part already assigned to the line of work in which they are most proficient.

4. Applicants should apply to the Surgeon General, Public Health Service, Washington, D. C.

In general, it may be stated that any application received in connection with the above will not be considered for grades higher than Passed Assistant Surgeon in the Reserve Corps, with corresponding grade and pay of a Captain in the Army.

Major Sam F. Seeley, Office of Defense Health and Welfare Services, wrote as follows:

In response to your letter of April 21, I have the following comments to offer in the order of the questions listed by you:

1. A limited number of dermatologists are needed by the armed services, but this number is so limited that I would be disinclined to encourage every dermatologist to believe that his duties would be strictly in that field.

2. From the above, there can be no assurance that dermatologists in general will be given assignments strictly in their field.

3. Those dermatologists well recognized in their specialty who are now in the military service must continue serving in their present capacity until such time as the Surgeon General has the advantage of an oversupply. I do not believe we are justified in asking the Surgeon General to make reassignments until the rest of the profession has come forward for service, thereby making such rearrangements feasible.

4. Dermatologists applying for a commission should emphasize their training and on the statement of preferences form should ask for assignment in their field.

In my presentation before medical groups, I frequently make a statement somewhat as follows:

"If you pediatrists feel somewhat let down that the Army has not provided subjects for your practice except in the case of infectious disease sections on large medical service, pity the poor obstetrician, who must enter military service and who will probably attend only the dystocia of field mortars."

We must, of course, realize that the primary requisite is that of a degree of medicine and only about 25 per cent have the opportunity of serving continuously in their own self-chosen specialty.

A statement which reached my office the other day has considerable merit, that as in the last war, many men who anticipate that their experience will make specialists out of general practitioners are going to have to be satisfied with having been made better practitioners if now engaged as specialists.

We must win this war, and then enjoy our highly developed specialization in peace time.

When an applicant applies directly to any Army installation for commission in the Army Medical Corps, he is referred to the Procurement and Assignment Service. When an applicant applies to any Navy commandant for commission in the Navy Medical Corps, his application is sent to the Bureau of Medicine and Surgery, and such names are cleared through the Procurement and Assignment Service before the commissions are granted, as also are applications for commissions in the Public Health Service. Therefore it is imperative that every applicant for a commission complete the questionnaire recently circulated. The central office of the Procurement and Assignment Service is located at 905 "E" Street, N. W., Washington, D. C. The executive officer is Major Sam F. Seeley, Medical Corps, United States Army.

500 Penn Avenue.

ABSTRACT OF DISCUSSION

DR. MARION B. SULZBERGER, New York: The Surgeon General of the Navy, in the letter which Dr. Guy read, has stated better than any one else could and more authoritatively just what attitude the Navy Medical Corps now takes toward specialists in dermatology and syphilology. Anything I say now will serve simply to underline his statements. It is the policy of the Navy at present to have combined departments of dermatology and syphilology in all the large naval hospitals. Not only is this an advantage to dermatologists and syphilologists, but I believe, and the Surgeon General believes that it presents a great step forward in the handling of this group of cases by the Naval Medical Corps. There is probably nothing more illogical than to have syphilis treated, as heretofore, by the urologist. Why should the urologist treat syphilis? Certainly the practicing urologists and those in hospitals and university medical schools have no experience whatsoever with syphilis, and certainly these are the physicians who are being called into military service to take care of the tremendous load in this emergency. In other words, the career military physicians represent a very small minority indeed among the physicians who have to take care of the military forces. So the supply of physicians who know anything about syphilis can certainly not come from the specialty of urology outside the armed forces. There is no logical reason why urologists should treat syphilis. Even though the lesion is penile—which it is for only a few weeks, as compared with the whole life span of the syphilitic patient—the change seen is in the skin of the penis; so the most important and earliest differential diagnosis is a dermatologic one as a rule. And as far as the urologist and generalized or visceral syphilis is concerned, I believe there are few who will contend that the general urologist uses the stethoscope or otoscope or ophthalmoscope more often than the dermatologist. Certainly the uses of the cystoscope in the diagnosis and management of syphilis are limited. Urology of today is usually a surgical specialty, and the urologist who is interested in anything except the surgical phase of urology is a great exception. Urologists as a rule do not purport to be or pretend to be syphilologists and are not trained in syphilology. In contrast to this, dermatologists in this country today must be both dermatologists and syphilologists in order to be recognized as specialists.

The incidence of cutaneous diseases in the armed forces is tremendous. They account for about 8 per cent of all the disabilities. In other words, about 12 patients out of every 100 have primarily a disease of the skin (this figure has nothing at all to do with the many additional patients in whom the cutaneous disease is incidental to some other disease, such as the man who is admitted to the hospital for appendicitis and is found to have athlete's foot or dandruff). The 8 per cent is composed of patients who are hospitalized or put on the sick list because of the cutaneous disease. Moreover, about 8 per cent of the total sick days are due to cutaneous diseases. Syphilis accounts for about another 6 or 7 per cent of the total. So about 15 per cent of the cases, or more than 1 in every 7, are within the specialty of dermatology and syphilology. As there are now 600 specialists certified by the American Board of Dermatology and Syphilology, the medical profession is ready to supply only a fraction of the percentage of dermatologists that would be necessary according to the relative numerical incidence of the diseases. Of course, this is not quite a fair basis of comparison, but it will give an idea of the amount of work which is to be done within this specialty.

I have heard it said that during times of this kind the military medical activities are not those in which research work can be done and interesting problems can be studied. I disagree with that statement. Of course the primary objective is to keep as many men behind as many guns as many days as possible, and that must always be borne in mind. But in doing that, many problems arise which must be studied now and cannot be studied at any other time. Consider, for instance, the damage produced by agents of chemical warfare. No one is going to concentrate on the study of this type of damage, its prevention and treatment, except in times like these. As soon as peace comes the interest in that phase of medicine naturally decreases to almost zero. Now the opportunity, money and material for studying the vesicant agents and their action on the skin are available. That problem certainly is, to a great degree, a dermatologic one. Now is the time to study burns and their treatment, to find quick, good ways of treating scabies effectively and of preventing it, to find the best ways to control pediculosis and to study the prophylaxis of venereal diseases and the best chemical and other methods of prevention and treatment. Nowhere is there the opportunity really to judge what prophylaxis is doing as well as in mass studies in the armed forces. When a man is at liberty for any time he always comes back to a medical officer; so one really can check up on what the prophylactic procedures are accomplishing. There is, for example, an actual question of whether the chemical prophylaxis now in use is of any value at all; and now is the time to follow that up and decide.

Another problem for study at present is the field of topical therapy. What is really known about topical therapy? What are the correct modern ointment bases to be given out to be used on the millions in the armed forces? What will keep? What will become moldy? What will penetrate? What is easily prepared? What is light in weight? What can be transported in simple, nonbreakable packages? What ointment base or powder or lotion can be prepared which saves critical materials? What can be used as a substitute for glycerin? What powders are the best to use? What is the best foot powder to control sweating and athlete's foot? What is the best foot powder to give millions of men who are going to sweat a great deal before this war is over? Certainly these men are going to have a high incidence of incapacity due to foot trouble, such as fungous infections and pyodermas. Who knows what is really the best in prevention and in treatment? Now is the time to find out, speedily and accurately.

DR. HOWARD FOX, New York: Dermatologists in the present war have certain advantages over those in the first world war. Their pay is higher and in my opinion generous. There is less chance that so many mistakes will be made in putting men in positions for which they are not fitted. Trained dermatologists, such as those certified by the American Board of Dermatology and Syphilology, are in favored positions, as the surgeons general of the Army and Navy have complete records of their ability and attainments. Many physicians fear they cannot learn much about dermatology in the military service and continue as at home to encounter interesting or rare cases and perhaps engage in research work. Dr. Sulzberger is correct in saying that there are numerous problems peculiar to warfare which can be studied. However, from my experience, a war is not conducive to serious study. There are too much restlessness and uncertainty as to when a man will be rooted up from the job he is holding and sent to a new station. If a dermatologist is fortunate in getting a good assignment, well and good. However, I do not think there will be enough good jobs to go around. At any rate, the principal aim for every one in this war is to win it, which means working unselfishly for Uncle Sam and doing what one is told.

It is unfortunate that refugee physicians cannot become officers in the Army until they have become full citizens, after at least five years' residence in this country, while in the Navy they must have been here for ten years. Major General Hershey urges these men to volunteer without delay as enlisted men. They will then be placed in the medical department, probably as noncommissioned officers. On account of the urgent need for medical officers, General Hershey thinks it will be only a short time before public opinion will demand a change in regulations allowing these men to become officers. I feel sure that many of them would like to serve their adopted country in this manner.

DR. DONALD M. PILLSBURY, Philadelphia: The Committee on Medicine of the National Research Council has been obtaining information regarding the incidence of disability from various dermatoses in the Army and Navy, the types of cutaneous disease most frequently encountered, and the steps which might be taken to reduce such disability. Almost 10 per cent of admissions to military hospitals are due to cutaneous disease. From personal observation, I am sure that in medium-sized or large Army hospitals one medical officer in fifteen can be kept extremely busy in the care of patients with diseases of the skin and syphilis. I feel that the offices of the surgeons general are cognizant of and sympathetic with the need for better care of cutaneous diseases.

Recently, under the auspices of the National Research Council, Lieutenant Commander Sulzberger, Major Livingood and I have been preparing a manual on the care of diseases of the skin. We have encountered some difficulty, since in the field it is necessary to determine what is the *single* best treatment, or at most the two best treatments, for a particular condition. As one reviews papers on dermatologic therapeusis, it is too often apparent that control studies have not been made to enable one to compare the effect of a particular new treatment with the results obtained with standard methods. Such studies are badly needed. A few problems to which there are no satisfactory answers are: (1) treatment of fungous infections, (2) combating the effects of hyperhidrosis, (3) prevention and treatment of weed dermatitis, (4) enhancing of effects of local treatment of pyoderma with sulfonamide compounds, (5) determining the relative value of newer methods in the treatment of scabies and pediculosis and (6) the physiology and control of itching. I agree with Dr. Sulzberger that, because of the conditions of control, hospitals of the Army and Navy are ideal places in which to compare the effects of various treatments.

Because of the importance of the skin in various war injuries, its reactions to vesicant gases, infection and burns, I think that at present there are a larger number of physiologists and chemists working with the skin than ever before, investigators who had previously regarded the skin with disinterest, if not distaste. I believe that as a result of the special methods and knowledge that these scientific workers will bring to bear on the problem knowledge of the physiology of the skin is going to be greatly increased, and I predict that many explanations for clinical problems will come out of these studies.

Dr. C. Guy Lane, Boston: In February I had the pleasure of hearing Colonel Lull and Major Seeley. Colonel Lull stated at that time that only 10 per cent of the physicians in the Army could be allocated to specialization, whereas in civil life the figure is 30 to 35 per cent. So it is not possible apparently for all specialists to stick to work in their own particular field. Colonel Lull also stated, as he said in the letter, that insofar as possible physicians would be assigned to their own specialties, at least after a while. At this meeting, which Dr. Guy also mentioned, there were representatives not only of the Army and of the Association of American Medical Colleges but, of course, of the Council of Medical Education of the American Medical Association and of various boards. At that time the medical situation was well straightened out with regard to the deferment of medical and premedical students. The question of postgraduate training was not straightened out. One can see the impossibility at present of allocating physicians for postgraduate study.

At this meeting a liaison committee was established to work with the Procurement and Assignment Service, the surgeons general and the Selective Service with regard to providing for a supply of interns for necessary graduate work in various hospitals, adequate care for the civilian population and a future supply for the Army and Navy, but the details of that plan have not yet been worked out.

There has been a definite attempt on the part of the American Board of Dermatology and Syphilology to cooperate and provide as much uniformity as is possible. So far as this board is concerned, there has been a great deal of correspondence and activity in regard to the military situation.

There is considerable interest with regard to the role of urology and syphilology, the dermatologist not having control of syphilis. I know of two or three camps in which the dermatologists have been able to obtain the syphilis work, owing to the fact that the urologist was not interested and had not been trained in the field. The Urologic Board does not examine in syphilis and does not require training in syphilis. There is a definite place for dermatologists in military service. The report of the Surgeon General from the last war shows four to five million days lost because of dermatologic conditions and syphilis; so there is certainly need in the armed forces during the present war for dermatologists trained in diagnosis, treatment and prevention of cutaneous diseases and syphilis.

Dr. Dudley S. Smith, Charlottesville, Va.: It has been reported by those in charge of the medical divisions of the services that among physicians entering (and probably among those already in) the service there are fewer well trained in dermatology than in any other branch of medicine. I think this gives an opportunity to persons interested in medical education, particularly those in charge of the administration of medical schools, to urge the granting of more facilities and a better curriculum for teaching this subject.

There is another subject that has not been mentioned much in this discussion. It is assumed that all of the dermatologic work will be done by trained dermatologists in the Army and Navy and other branches of the armed forces. As a matter of fact, most of this work will necessarily have to fall on physicians who are not trained dermatologists.

DR. WILLIAM H. GUY, Pittsburgh: I have been asked regarding the position of younger physicians—not full time dermatologists—in relation to military appointments in dermatology. I suggest to them that in making their applications they state their qualifications, and if there are positions for them they will certainly be assigned.

I have also been asked regarding the status of dermatologists in base hospitals. That has been touched on by Dr. Lane and others in the discussion. It is largely up to the commander of the hospital as to his duties and whether or not syphilis is included.

VITAMIN THERAPY IN DERMATOLOGY AND SYPHILOLOGY

PAUL A. O'LEARY, M.D.
ROCHESTER, MINN.

Vitamins have now been employed long enough in the treatment of cutaneous diseases to warrant an appraisal of their clinical value. After the work of Goldberger, Wheeler and Tanner [1] on pellagra, there were no outstanding contributions on the relation of vitamin deficiency to diseases of the skin until the present wave of enthusiasm developed several years ago. It now appears that there are six dermatoses attributable to vitamin deficiency, and there are indications that in the near future several other diseases with cutaneous manifestations will be found to be the result of an avitaminosis.

This survey is a clinical appraisal of the value of vitamin therapy in dermatology and syphilology based on my own experience and on well controlled studies reported in the literature. I have omitted the reports of single cases in which the patients were benefited by a hit and miss type of vitamin therapy, and the review of the literature has been limited to recent reports of experimental work and well controlled clinical observations.

Table 1 is a crystallization of the present day information on the degree of improvement produced by vitamin therapy in the practice of dermatology and syphilology, while table 2 summarizes the results reported in the literature and my own observations of the effects of the same type of therapy on a variety of dermatoses and on a few of the complications of syphilis.

It is evident in certain diseases of the skin associated with clinical signs of avitaminosis that after the supplemental use of the vitamin or vitamins, either by proper diet or by the administration of a synthetic form of the necessary vitamin, the cutaneous signs of the disease disappear. In some of the diseases this response is so rapid and clearcut that the deduction is warranted that the result is "specific." These

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From the Section on Dermatology and Syphilology, the Mayo Clinic.

Read at the Fourth Annual Meeting of the American Academy of Dermatology and Syphilology, New York, Dec. 14, 1941.

1. Goldberger, J.; Wheeler, G. A., and Tanner, W. F.: Yeast in the Treatment of Pellagra and Black Tongue, Pub. Health Rep. **40**:927-928 (May 8) 1925.

diseases include pellagra,[2] ariboflavinosis or cheilosis,[3] phrynoderma,[4] pityriasis rubra pilaris,[5] keratosis follicularis [6] and the so-called seborrheids recently described by Gross.[7]

There is another group of diseases in which the results of the use of vitamin therapy are less pronounced, do not appear in all of the cases and are less conclusive. This group includes lichen spinulosus, keratosis pilaris, senile vaginitis, monilia infections, rosacea keratitis, psoriasis, acne cachecticorum and "dry skin."

TABLE 1.—*Current Conception of the Value of Vitamin Therapy in Dermatology and Syphilology*

	Vitamin Employed	Supplementary Vitamin	Result Expected*	Natural Sources of Vitamin
Dermatoses				
Acne, severe	B complex, nicotinic acid and D		2	Yeast, cod liver oil and viosterols
Acrodynia	B_1 complex and D		0-2	Yeast, liver, cod liver oil, peanut butter and oil
Ariboflavinosis	Riboflavin		4	Yeast, peanut oils, milk, meat, citrus fruits, tomatoes and fruit juices
Arsphenamine dermatosis (preventive)	C		1-2	
Cheilosis	Riboflavin		4	
Herpes zoster	Thiamine		1	
Keratosis follicularis	A		3-4	Liver, milk, eggs, butter and vegetables
Keratosis pilaris	A		3-4	
Lichen spinulosus	A		2-3	
Lichen planus	B complex		0-1	
Monilia infections	B complex		2	
Pellagra	Nicotinic acid	Thiamine and riboflavin	4	Yeast, peanut oil and butter
Pityriasis rubra pilaris	A		3-4	
Pityriasis-rubra-pilaris-like syndrome	A		3-4	
Phrynoderma	A		3-4	
Rosacea keratitis	Riboflavin		2	
Scurvy	C		3-4	
Seborrheids	B complex		3	
Roentgen ray sickness	Thiamine		1	
Syphilis				
Tabes dorsalis	Thiamine		0-1	
Lightning pains	Thiamine		0-1	
Crises	Thiamine		0-1	
Tryparsamide treatment	Thiamine		0-1	
Atrophy of the optic nerve	Thiamine		0-1	
Interstitial keratitis	Thiamine		...	

* On the basis of 0 to 4, 4 denotes maximal benefit and 0 denotes no benefit.

2. Spies, T. D.: Pellagra, in Cecil, R. L.: A Textbook of Medicine, ed. 5, Philadelphia, W. B. Saunders Company, 1940, pp. 624-631.

3. Sebrell, W. H., and Butler, R. E.: Riboflavin Deficiency in Man: A Preliminary Note, Pub. Health Rep. **53**:2282-2284 (Dec. 30) 1938.

4. Frazier, C. N., and Hu, C. K.: Cutaneous Lesions Associated with a Deficiency of Vitamin A in Man, Arch. Int. Med. **48**:507-514 (Sept.) 1931.

5. Brunsting, L. A., and Sheard, C.: Dark Adaptation in Pityriasis Rubra Pilaris, Arch. Dermat. & Syph. **43**:42-59 (Jan.) 1941.

6. Peck, S. M.; Chargin, L., and Sobotka, H.: Keratosis Follicularis (Darier's Disease): A Vitamin A Deficiency Disease, Arch. Dermat. & Syph. **43**:223-229 (Feb.) 1941.

7. Gross, P.: Nonpellagrous Eruptions Due to Deficiency of Vitamin B Complex, Arch. Dermat. & Syph. **43**:504-531 (March) 1941.

The third group consists of those diseases in which vitamin therapy has been reported to be of value but in which results have not been confirmed by subsequent observations. It includes dermatosclerosis, epidermolysis bullosa, arsphenamine dermatitis (preventive therapy), lichen planus, acrodynia, herpes zoster and roentgen ray sickness. In this group may also be included some of the late complications of syphilis in which vitamin therapy was found to be of no value, namely, the lightning pains and gastric crises of tabes dorsalis and interstitial

TABLE 2.—*Results Obtained with Vitamin Therapy in Dermatology and Syphilology*

	Degree of Improvement		
Vitamin	Definite	Moderate to Slight	Insignificant to None
Vitamin A	Keratosis follicularis, pityriasis rubra pilaris, pityriasis-rubra-pilaris-like syndrome and phrynoderma	Senile vaginitis, lichen spinulosus, keratosis pilaris, "dry skin" and "dry hair"	
Vitamin B complex	Pellagra and seborrheids	Monilia infections and acne cachecticorum	Lichen planus
Thiamine (B_1)	.....	.....	Lightning pains and gastric crises of tabes dorsalis, tryparsamide treatment, acrodynia, herpes zoster and roentgen ray sickness
Nicotinic acid	.....	.....	Acne
Riboflavin (B_2)	Cheilosis and ariboflavinosis	Rosacea keratitis	Interstitial keratitis
Pyridoxine (B_6)	.....	.....	
Pantothenic acid	.....	.....	Canities (?)
Ascorbic acid (C)	Scurvy	.....	Arsphenamine dermatosis (preventive)
Vitamin D	.....	Pustular and exfoliative psoriasis, psoriatic arthritis, acne vulgaris and pemphigus	Scleroderma and epidermolysis bullosa
Vitamin E	.....	.....	Dermatomyositis

keratitis. This therapy also is of little value in the prevention of optic complications of tryparsamide therapy.

Emphasis is warranted by the fact that in the treatment of cutaneous manifestations the most pronounced improvement following vitamin therapy occurs in patients in whom constitutional signs of avitaminosis also are present. It also is well to emphasize the fact, as shown in the tables, that for certain of these patients the use of more than one vitamin may be necessary.

The ill effects of vitamin therapy on the skin are rather conspicuous by their absence. Mitchell [8] has observed that a toxic erythema developed in 2 patients who had taken vitamin B complex for a long

8. Mitchell, J. H.: Personal communication to the author.

time. The erythema cleared up when administration of the vitamin B complex was stopped and reappeared when it was begun again. I have encountered 1 similar case.

A review of the literature on the use of vitamins in the practice of dermatology reveals many differences of opinion as to the value of a single vitamin or a combination of vitamins in the treatment of certain diseases of the skin. These discrepancies are equally prominent in the transactions of the dermatologic societies in this country. I have briefly enumerated some of the reasons why these differences in opinion occur and also shall include a few explanations of why vitamin therapy does not always control the diseases reported as due to vitamin deficiency. The personal equation of the physician, the lack of control cases, inexperience in dermatology and the "enthusiasm of youth" account for some of the favorable observations reported in the literature which subsequently have not been substantiated by other investigators. On the other hand, these difficulties are not entirely due to the physician's inexperience, and this was especially true in the early experience with many of the synthetic vitamin preparations, as frequently the amount of vitamin or vitamins contained in a capsule was insufficient, the statement of unitage was misleading or the vitamin was inert. This was especially true of those preparations which contained many vitamins in the same capsule; the number of units of a vitamin was often far below the desired and required amount. Likewise, it was not known then (nor has there been much increase in the knowledge during the past few years) what are the daily vitamin requirements of normal persons. At present these requirements are being established.

The evidence now indicates that under certain conditions vitamins to be effective must be in harmony or in combination, as, for example, in cases of pellagra, in which the simultaneous use of nicotinic acid, thiamine and riboflavin is necessary to control the disease. I have the impression that some other diseases, such as psoriasis, which up to the present have shown varying degrees of improvement from vitamin therapy may be completely controlled when the proper combination of vitamins is found. Not only is it essential that the required combination of vitamins be present, but it is necessary that the vitamins be in proper ratio one to another.

It is apparent from the work in the laboratory as well as from clinical experience that there are many factors that inhibit complete absorption of vitamins after the patient swallows them. The following are some of the reasons for inadequate absorption[9]: The coating of

9. Andersen, O.: Untersuchungen über die Wirkung von Paraffinöleingabe auf die Resorption des A-Vitamins bei Menschen, Acta pædiat. **24**:422-427, 1939.

the intestinal tract by liquid petrolatum used either as a vehicle or taken independently may inhibit the absorption of vitamins. In the presence of disease of the viscera, of the intestines or, especially, of the liver, the vitamins may not be properly converted and accordingly may "overflow" rather than be absorbed. Similarly, because of disease of the liver the vitamin may not be converted and hence not be stored. Mackie, Eddy and Mills [10] have summarized their opinion as follows: "Any condition which interferes with the normal intake of food, normal digestion, normal absorption of the products of digestion and normal utilization of these products by the liver may produce secondary or conditioned avitaminosis." Comment has already been made on the fact that knowledge as to the daily requirements of the various vitamins both of normal persons and of persons with avitaminosis is in the process of being accumulated at this time. A toxemia may lead to the development of signs of a deficiency disease by interfering with the function of the enzyme in which the vitamin acts. The absence or decrease of gastric juice may inhibit the synthesizing of the coenzymes, and, in fact, anything that inhibits the action of an enzyme may interfere with the absorption process of the vitamins.[11] Alkalosis, water intoxication and diarrheal states lead to deprivation of vitamins.[12]

Other factors that modify the results of vitamin therapy are the use of the synthetic vitamins versus vitamins obtained from natural sources. It has been said often, but is still worthy of repeating for emphasis, that the best place to obtain vitamins is in the grocery store rather than in the drug store. However, occasional cases are encountered in which the use of the synthetic products is necessary.

It has been known for some time that certain persons will demonstrate clinical signs of avitaminosis even though eating a wholesome diet similar to that partaken of by other members of their family who do not show signs of vitamin deficiency. My attention was called to such patients in 1928,[13] when I observed a group of pellagrins who were residents of the northwest part of the United States and the midwestern part of Canada. The cause of the inability of these persons to utilize vitamins was not demonstrated then, although most of them

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10. Mackie, T. T.; Eddy, W. H., and Mills, M. A.: Vitamin Deficiencies in Gastrointestinal Disease, Ann. Int. Med. **14**:28-41 (July) 1940.

11. Von Euler, H., and Zoudek, B.: Stabilität des Prolans; ein Hinweis auf seine enzymatische Natur, Skandinav. Arch. f. Physiol. **68**:232-244, 1934.

12. (*a*) Rosenblum, L. A., and Jolliffe, N.: The Oral Manifestations of Vitamin Deficiencies, J. A. M. A. **117**:2245-2248 (Dec. 27) 1941. (*b*) Bean, W. B., and Spies, T. D.: Vitamin Deficiencies in Diarrheal States, ibid. **115**: 1078-1081 (Sept. 28) 1940.

13. O'Leary, P. A.: Pellagra: A Study of Thirty-Four Cases in Localities Where Pellagra Is Not Endemic, Northwest Med. **27**:319-323 (July) 1928.

overcame the avitaminosis when their diets were amplified and supplemented with additional vitamins. There was another group of pellagrins observed at the same time who had mechanical obstruction or dysfunction of their gastrointestinal tracts which prohibited the ingestion or retention of adequate amounts of food. These patients had malfunctioning gastroenteric anastomoses, esophageal strictures, carcinoma of the cardiac end of the stomach, and so forth. When the constant regurgitation of food and the mechanical interference with eating were corrected surgically, the signs of pellagra disappeared, if the patient was able to withstand the severe exacerbation of the pellagra that followed the operation.

It would appear that some of the overly enthusiastic reports about the value of vitamin therapy in the treatment of diseases of the skin have been observed in cases in which the patients did not have a true avitaminosis but rather presented a syndrome resembling it, which was in reality a pseudoavitaminosis. This disappeared as the result of time or some therapeutic agent rather than as a result of the administration of additional vitamins. Comment has been made on numerous occasions that the patient with cutaneous disease who is likely to improve after the administration of vitamins in one form or another is the one who likewise demonstrates clinical signs of vitamin deficiency. In fact, according to my experience at the Mayo Clinic, it is indeed rare that vitamin therapy will produce much improvement in a disease of the skin if the constitutional signs of avitaminosis are absent.

The points I have called attention to thus far are but a few of the reasons why there are considerable confusion and much skepticism in the minds of many dermatologists who have anticipated striking therapeutic results from vitamin therapy but who have been repaid instead with therapeutic failures. The variations in the reports in the literature as to the value of vitamin therapy in certain diseases of the skin have augmented the dermatologist's skepticism, especially when in his own practice the clinical failures have far outnumbered the successes. Although vitamin therapy is not new, it has become popular rapidly during the past few years, so fast, in fact, that few physicians have familiarized themselves with its developments and its limitations. As a result, a "shotgun" type of effort, with most of the vitamins included in one capsule, has led to many clinical disappointments. On the other hand, when a patient with avitaminosis and associated lesions of the skin is given the additional vitamins he or she requires, the therapeutic result is sometimes startling to the physician and usually comforting to the patient.

At the time of writing this paper, it appears that the near future will bring other significant developments in the use of vitamin therapy in dermatology. During the past year two diseases, namely, pityriasis rubra pilaris and keratosis follicularis, have been found to be associated

with avitaminosis, and several new syndromes of vitamin deficiency with cutaneous manifestations have been described. The lesions of the mucous membrane and skin in cases of ariboflavinosis were described in 1938.[3] In the interim, while the results of continued laboratory and clinical investigations are awaited, it would seem advisable to maintain an open opinion on the value of vitamins in dermatology, to learn the clinical signs of avitaminosis and not to expect that "shotgun" prescriptions of vitamins will be a panacea for the vague and indefinite dermatoses. Also caution and experience in the use of vitamins as well as in the practice of dermatology are necessary in interpreting in terms of human skin the changes that occur from dietetic experiments in the pelt of the laboratory animal. Although the disappointments from the clinical trials of vitamin therapy in dermatology have been many, it is now known that six cutaneous diseases are associated with avitaminosis and that seven other diseases are remotely or indirectly attributable to vitamin deficiency, and of course there is the hope that the future will reveal other dermatoses to be of similar origin.

SUMMARY

At present the cutaneous diseases that have been shown to be due to vitamin deficiencies are pellagra, ariboflavinosis or cheilosis, phrynoderma, pityriasis rubra pilaris, keratosis follicularis and certain types of seborrheids. There is another group of cutaneous diseases in which the results of the use of vitamin therapy are not as "specific," in that in most of the cases improvement in the cutaneous lesions is less pronounced or may not appear in all cases. Included in this group are lichen spinulosus, keratosis pilaris, senile vaginitis, monilia infections, rosacea keratitis, psoriasis, acne cachecticorum and "dry skin." Diseases of the skin in which no improvement of note was observed, although reports had indicated that they were benefited by certain types of vitamin therapy, include dermatoscleroses, epidermolysis bullosa, arsphenamine dermatitis (preventive therapy), lichen planus, acrodynia, herpes zoster and roentgen ray sickness. No significant benefit was obtained with vitamins in the various manifestations of syphilis. The most pronounced benefits were noted in cases in which the dermatoses were associated with constitutional signs of avitaminosis. Also, in certain cases the use of more than one vitamin was found to be necessary. Comment is made on some of the reasons why discrepancies in the literature and differences of opinion occur as to the value of vitamin therapy in dermatology.

PHYTOPHARMACOLOGIC REACTIONS OF BLOOD FOLLOWING TREATMENT WITH SULFANILAMIDE AND DERIVATIVES

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Cutaneous reactions are among the commonest toxic manifestations following administration of sulfanilamide and its derivatives, and as therapy with these drugs expands new toxic effects of this type are revealed. Certain of these compounds, particularly sulfathiazole,[1] appear to be more liable than others to induce dermatoses. Such reactions, however, have been described as occurring after administration of all the compounds. Thus, cyanosis, jaundice, erythema and dermatitis have been observed, and even scarlatiniform, morbilliform and purpuric eruptions may develop after treatment with sulfanilamide.[2] Acute exfoliative dermatitis with fatal outcome following the administration of sulfathiazole was described by Weinstein and Domm.[3] Loveman and Simon[4] noted erythema nodosum after sulfanilamide therapy. Vesicular eruptions were mentioned by Menville and Archinard.[5] Other dermatoses occurring after sulfanilamide therapy were described by Tedder.[6] Among the graver dermatologic lesions following the administration of these chemotherapeutic agents are eruptions of a pemphigoid type. Wien and Lieberthal[7] described pemphigus foliaceus following use of sulfanilamide and sulfapyridine. Again, Epstein[8]

From the Pharmacological Research Laboratory, Hynson, Westcott & Dunning, Inc.

1. Geiling, E. M. K.: Illinois M. J. **78**:404, 1940.

2. Spink, W. W.: Sulfanilamide and Related Compounds in General Practice, Chicago, The Year Book Publishers, Inc., 1941.

3. Weinstein, M., and Domm, A. H.: Development of Acute Exfoliative Dermatitis During Administration of Sulfathiazole, J. A. M. A. **117**:607 (Aug. 23) 1941.

4. Loveman, A. B., and Simon, F. A.: J. Allergy **12**:28, 1940.

5. Menville, J. G., and Archinard, J. J.: Skin Eruptions in Patients Receiving Sulfanilamide, J. A. M. A. **109**:1008 (Sept. 21) 1937.

6. Tedder, J. W.: Toxic Manifestations in Skin Following Sulfanilamide Therapy, Arch. Dermat. & Syph. **39**:217 (Feb.) 1939.

7. Wien, M. S., and Lieberthal, E. P.: Pemphigus Foliaceus-Like Eruption Following Use of Sulfanilamide and Sulfapyridine, J. A. M. A. **117**:850 (Sept. 6) 1941.

8. Epstein, E.: Bullous Eruption Following Sulfanilamide Therapy, Arch. Dermat. & Syph. **41**:61 (Jan.) 1940.

discoursed on the bullous eruptions occurring after treatment with sulfanilamide. Loveman and Simon [9] noted bullous stomatitis after such therapy, and similar eruptions were reported by Bettley and Simon.[10] Caro,[11] who introduced sulfanilamide in the treatment of pemphigus, has been confronted with the possibility that such therapy may cause bullae to develop on apparently normal skin, an observation confirmed by the complication occurring in the case reported by Feldman.[12] Holland [13] claimed that pemphigus instead of being ameliorated may be aggravated by administration of sulfanilamide. Omens and Robbins [14] reported toxic bullous eruptions following the use of sulfapyridine, and reports of other such pemphigoid reactions may be gleaned from more recent comprehensive reviews.

CUTANEOUS REACTIONS FOLLOWING ADMINISTRATION OF SULFONAMIDE COMPOUNDS

It was particularly in connection with the pemphigoid dermatoses succeeding administration of sulfanilamide and its derivatives that the present study was undertaken. Pemphigus has proved an enigma to physicians from time immemorial. Until the phytopharmacologic researches of Macht and Pels, initiated in 1927 [15] and continuing until the present day, nothing definite was known concerning the cause of this disease. In 1927 these authors commenced an extensive and comprehensive study of phytotoxic reactions of blood serums from patients with all kinds of dermatoses. As the earlier phytopharmacologic studies of Macht and his associates [16] revealed that minute quantities of toxic substances not demonstrable by zoopharmacologic methods could be detected in serums of certain patients by means of delicate, plant-physiologic tests, it was deemed worth while to examine blood serums from patients with various dermatoses in the hope of observing quantitative differences in respect to their effect on living seedlings. Thus it was discovered that the blood serum and vesicular fluid of

9. Loveman, A. B., and Simon, F. A.: Fixed Eruption and Stomatitis Due to Sulfanilamide, Arch. Dermat. & Syph. **40**:29 (July) 1939.

10. Bettley, F. R., and Simon, P.: Brit. M. J. **1**:1177, 1939.

11. Caro, M. R.: Pemphigus: Treatment with Sulfanilamide, Arch. Dermat. & Syph. **37**:196 (Feb.) 1938.

12. Feldman, S.: Pemphigus Treated with Sulfanilamide: Sulfanilamide Eruption, Arch. Dermat. & Syph. **39**:601 (March) 1939.

13. Holland, M., in discussion on Feldman.[12]

14. Omens, D. V., and Robbins, J. B.: Severe Toxic Bullous Eruption Following the Use of Sulfapyridine, Arch. Dermat. & Syph. **40**:633 (Oct.) 1939.

15. Macht, D. I., and Pels, I. R.: Proc. Soc. Exper. Biol. & Med. **25**:237, 1927.

16. Macht, D. I., and Lubin, D. S: J. Pharmacol. & Exper. Therap. **22**:413, 1924. Macht, D. I., and Anderson, W. T.: ibid. **34**:365, 1928.

patients with pemphigus exhibited a decided toxicity for roots of Lupinus albus seedlings grown under standardized conditions and furthermore that such a phytotoxic effect was exerted by serums from patients with but few other diseases characterized by cutaneous eruptions. During the past ten years nearly 3,000 specimens of blood from patients suspected of having pemphigus have been subjected to the Macht-Pels test, and, although I examined the serums with no prior knowledge of the patients' histories or diseases, the diagnosis made on the basis of the phytopharmacologic test was proved remarkably accurate by the subsequent histories of patients whose blood was studied.[17]

Since distressing bullous lesions sometimes follow administration of the sulfanilamide compounds, I wished to determine whether specimens obtained from patients with such pemphigus-like bullae exhibited the same phytotoxic reaction as those from patients with bona fide pemphigus. The present study was therefore begun with examination of specimens secured from both lower animals and man after oral administration of sulfanilamide or one of its derivatives.

MATERIALS STUDIED

I studied the phytopharmacologic effects of the following compounds:[18] (1) sulfanilamide, (2) azosulfamide, (3) sulfathiazole, (4) sulfapyridine, (5) sulfadiazine, (6) sulfaguanidine and (7) succinylsulfathiazole. Three distinct series of experiments were made. In the first series, 0.5 Gm. and also 1.0 Gm. doses of the respective drugs were administered by stomach tube to adult rabbits weighing 2 to 3 Kg. Such doses ensure a concentration of the drugs in the blood of animals that is comparable with that effected in the blood of human beings receiving full doses of the compounds; indeed, it was usually greater. This finding was definitely established by standard biochemical tests. Table 1 will furnish some idea of the concentrations (determined by a modification of the method of Bratton and Marshall[19]) of the four

17. Pels, I. R., and Macht, D. I.: Phytopharmacologic Examination of Blood in Pemphigus and Some Other Diseases of the Skin, Arch. Dermat. & Syph. **19:** 640 (April) 1929; Phytopharmacology of Pemphigus and Other Dermatoses: Additional Studies, ibid. **23:**601 (Sept.) 1931. Macht, D. I.: Acta dermat. **18:** 126, 1932.

18. The chemical designations of these compounds are as follows: (1) sulfanilamide, paraaminobenzenesulfonamide; (2) azosulfamide, disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydronaphthalene-3′,6′-disulfonate; (3) sulfathiazole, 2-(paraaminobenzenesulfonamido)-thiazole; (4) sulfapyridine, 2-(paraaminobenzenesulfonamido)-pyridine; (5) sulfadiazine, 2-(paraaminobenzenesulfonamido)-pyrimidine; (6) sulfaguanidine, sulfanilylguanidine; (7) succinylsulfathiazole, succinyl-2-(paraaminobenzenesulfonamido)-thiazole.

19. Bratton, A. G., and Marshall, E. K., Jr.: J. Biol. Chem. **128:**537, 1939.

principal compounds in the blood of rabbits. Specimens of normal blood were drawn before administration of the drugs, and other specimens were obtained six and twenty-four hours after. The blood was centrifuged and the serum then tested by the technic to be described. In the second series, blood serum was obtained from patients treated with various compounds. The specimens obtained after such administration were compared with specimens of normal blood serum as controls with regard to their effect on growth of Lupinus seedlings. In the third series, the effect of various concentrations of the respective compounds in plant-physiologic saline solution was compared with that of controls on seedlings grown under identical conditions.

METHOD OF STUDY

The phytopharmacologic technic requires no long exposition here, as it has been described in great detail by my associates and myself in numerous publications.[20]

TABLE 1.—*Concentration of Sulfonamide Compounds in the Blood of Rabbits After the Administration of the Drugs in Doses of Five-Tenths Gram (Feb. 18-19, 1942)*

Rabbit	Weight, Kg.	Compound	Mg. per 100 cc. Blood	
			6 Hours	24 Hours
1	1.7	Sulfanilamide	8	3.0
2	2.7	Sulfapyridine	8	2.7
3	3.0	Sulfathiazole	17	3.0
4	2.4	Sulfadiazine	17	2.5

Briefly, seedlings of Lupinus albus, large variety, are germinated in finely divided sphagnum moss containing an optimum percentage of moisture. When the seedlings have attained a root length of from 35 to 50 mm. they are ready for the test. One series of these is placed in plant-physiologic saline solution while another series of plants from the same crop is grown in similar solution to which 1 per cent of the serum to be tested is added. All the plants are then allowed to grow at a temperature of 20 C. for twenty-four hours in the dark. At the end of that period the elongation of the control roots is compared with that of the seedlings placed in the serum solutions. The inhibition or stimulation produced by the unknown solution is expressed by the so-called index of growth, which is obtained by dividing the growth in the unknown solution by the normal increment in control solution. The formula for the index of growth, or phytotoxic index, is therefore $\frac{X}{N}$. In ordinary tests at least ten seedlings are used, but generally a larger number is employed for investigative purposes. Experiments are repeated on consecutive days, and an average is made of all the readings obtained of any unknown chemical or blood serum.

20. Macht, D. I., and Grumbein, M. L.: Arch. internat. de pharmacodyn. et de thérap. **60**:95, 1938. Macht, D. I., and Livingston, M. B.: J. Gen. Physiol. **4**:573, 1922.

The phytopharmacologic test as developed in this laboratory is remarkably accurate, and certainly the results obtained thereby are more reliable than the data derived by the usual zoopharmacologic methods, because of the far greater number of individual test objects that may be employed. Although the technic demands considerable knowledge of both pharmacology and plant physiology, in experienced hands it is easily performed. The data secured by this means have proved their reliability even when subjected to intensive statistical analysis by mathematical methods.[21] Results obtained from such examination of nearly 3,000 specimens of blood for pemphigus toxin not only proved statistically valid but completely agreed with the final clinical and pathologic diagnoses in such cases. An interesting illustration of this agreement between laboratory and clinical diagnosis has recently been published by Gellis and Glass [22] in a survey of 170 patients admitted to Bellevue Hospital, in New York.

RESULTS

Thirty experiments each were made with (1) blood serums of rabbits, (2) blood from patients treated with various sulfonamide compounds and (3) aqueous solutions of these chemicals. All the tests were performed on Lupinus albus seedlings grown for twenty-four hours in the dark at a temperature of 20 C. In each series all the specimens of blood, chemical solution or controls were subjected to exactly the same environmental conditions. In every case, the length of the roots at the beginning and end of the experiment was measured by the same individual, and the phytotoxic indexes were determined according to the formula just given, index $= \frac{X}{N}$.

Table 2 gives the phytotoxic indexes obtained with rabbit serums, 1 per cent, and solutions of the various drugs. These figures show the reactions exhibited at the end of twenty-four hours, but similar results were effected by blood serums drawn six to twelve hours after administration of the drugs. None of the indexes was less than 70 per cent, a significant finding, since the phytotoxic index of normal human blood, and indeed of the blood of all warm-blooded animals, drawn after administration of these compounds may therefore be regarded as exhibiting no more toxicity than those of normal rabbit serums; in fact, the specimens taken from these animals after treatment are often less toxic than normal rabbit bloods.

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21. Macht, D. I., and Macht, M. B.: J. Lab. & Clin. Med. **26**:597, 1941.

22. Gellis, S., and Glass, F. A.: Pemphigus: Survey of One Hundred and Seventy Patients Admitted to Bellevue Hospital from 1911 to 1941, Arch. Dermat. & Syph. **44**:321 (Sept.) 1941.

Table 2 also shows the phytotoxic indexes obtained with blood serums from human patients who have been under treatment with sulfanilamide or one of its derivatives. According to the records of clinicians from whom the specimens were obtained, in all the specimens of serum the usual therapeutic amounts of the drugs were detected. Here again all the indexes rose higher than the normal phytotoxic readings effected by human blood serums (70 to 75 per cent), and here, as in case of the rabbit serums, sulfanilamide was responsible for the

TABLE 2.—*Effect on Lupinus Seedlings of One Per Cent Solution of Serums of Rabbits and Patients After Administration of Sulfonamide Compounds*

Drug Administered	Phytotoxic Index (Per Cent)	
	Rabbits	Patients
Sulfanilamide	79	76
Sulfapyridine	86	94
Sulfathiazole	81	77
Sulfadiazine	83	85
Sulfaguanidine	79	83
Succinylsulfathiazole	81	78
Azosulfamide	96	..

TABLE 3.—*Effect of Various Dilutions of Aqueous Solutions of Sulfanilamide and Its Derivatives on Growth of Lupinus Seedlings*

Drug	Concentration	Phytotoxic Index (Per Cent)
Sulfanilamide	1: 10,000	83
Sulfanilamide	1:100,000	86
Sulfanilamide	1:250,000	112
Sulfathiazole	1: 10,000	86
Sulfathiazole	1:100,000	90
Sulfathiazole	1:250,000	118
Sulfapyridine	1: 10,000	88
Sulfapyridine	1:100,000	94
Sulfapyridine	1:250,000	130
Sulfadiazine	1: 10,000	87
Sulfadiazine	1:100,000	113
Sulfaguanidine	1: 10,000	114
Succinylsulfathiazole	1: 10,000	113
Azosulfamide	1: 10,000	137

figure nearest the normal average, while with some of the other compounds the blood serums were less toxic than normal specimens.

Table 3 shows the effect of aqueous solutions of the various drugs on the root growth of Lupinus albus seedlings. In these experiments the figures given by sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine—83, 88, 86 and 87 per cent, respectively—indicated but little toxicity, as evidenced by slight inhibition of growth of the seedlings. On the other hand, sulfaguanidine, succinylsulfathiazole and azosulfamide actually stimulated the plant growth, all the indexes being above 100 per cent. This finding does not surprise the experienced plant physiologist, as numerous phytopharmacologic investigations have

revealed that many drugs or chemicals have a diphasic action on plants, large doses being toxic and small doses definitely beneficial, stimulating growth or causing other physiologic activity. Accordingly I tested the effect of the various compounds on the growth of seedlings in higher dilutions of the drugs. The results obtained are also exhibited in table 3, where it can be seen that the four compounds which in 1 : 10,000 solution were mildly inhibitory, actually stimulated root growth when employed in greater dilution, e. g. 1 : 250,000.

COMMENT

It is evident from the data submitted that aqueous solutions of sulfanilamide and some of its derivatives and the serums from animals and from human beings treated therewith exert little or no toxic effect on growth of the Lupinus albus seedlings employed in the present investigation. According to the abundant data obtained by Macht and his co-workers the phytotoxic index of the normal blood serums of both man and mammals varies from 70 to 75 per cent. In all the experiments made with sulfonamide compounds the various serums studied gave higher readings than the normal average, the lowest figure of all the series being effected by sulfanilamide itself. These results are not surprising, because similar effects have been observed in certain physiologic and pathologic conditions. Atoxic blood serum, that is, blood serum showing less toxicity than normal for growth of Lupinus albus seedlings, is obtained from patients with certain diseases, especially virus diseases.[23] It is generally accepted that the ordinary germicides or antiseptics are poisonous for fungi and lower plants as well as higher forms of plant life; indeed, there have been authors who for purposes of orientation employed, for instance, suspensions of yeast to gage the possibly antiseptic tendency of various chemicals. In this sense of the word, the sulfanilamide compounds act in anomalous fashion. The exact nature of the mechanism of action of sulfanilamide and its derivatives, as Perrin Long [24] has stated, is still not entirely understood. Bullous eruptions occurring during therapy with these drugs do not indicate a true pemphigus and can be distinguished from such dermatoses by means of the phytopharmacologic test.

In conclusion, I wish to refer to the researches of Prof. John M. Beal,[25] in which, as he reported before the American Association for the Advancement of Science, sulfanilamide promoted evolutionary changes in plant growth similar to those effected by colchicine. Carl

23. Macht, D. I., and Gardner, R. E.: Proc. Nat. Acad. Sc. **22**:384, 1936. Macht, D. I.: Protoplasma **27**:1, 1937.

24. Long, P. H.: Sigma Xi Quart. **29**:149, 1941.

25. Beal, J. M.: Science News Letter **40**:373, 1941.

Lamanna's interesting communication [25] bearing on the findings reported in the present paper appeared in *Science,* March 20, 1942. This investigator reported stimulation of growth of various bacteria by sulfanilamide in low concentration. My findings concerning the growth-stimulating property of sulfanilamide and its derivatives for Lupinus albus seedlings constitute but another phase of the plant-physiologic phenomena wrought by these drugs.

SUMMARY

The effect on the root growth of Lupinus albus seedlings of blood serums from rabbits and human beings treated with sulfanilamide and some of its derivatives was studied.

These serums were generally found to be less toxic than normal rabbit or normal human serums.

Thus the phytopharmacologic reaction admits of the differentiation of certain dermatoses occurring after administration of sulfonamide compounds, particularly of eruptions of pemphigoid type from true pemphigus.

Aqueous solutions of sulfanilamide and derivatives of it in plant-physiologic saline solution exert a diphasic action on Lupinus albus seedlings, weak solutions stimulating and stronger solutions inhibiting root growth.

Dr. Tobias Weinberg and Dr. Harvey Fuller, of Mount Sinai Hospital, Dr. Solomon Sherman, of West Baltimore Hospital and Dr. Palmer Futcher, of Johns Hopkins Hospital, furnished blood specimens from patients treated with the compounds studied.

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26. Lamanna, C.: Science **95**:304, 1942.

GENERALIZED MONILIASIS WITH PROVED PATHOGENICITY

REPORT OF A CASE

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AND
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NEW YORK

The capacity of certain fungi to vegetate harmlessly on human skin (saprophytic or nonpathogenic state) is now generally admitted. Benham and Hopkins [1] and many investigators outside of the United States have recovered various species of Monilia and other yeastlike fungi from the healthy skin of normal persons. Because of this universality the finding of Monilia in scrapings from diseased skin does not necessarily establish that fungus as the etiologic agent. But Monilia is a facultative fungus in that it possesses the capability of assuming a pathogenic role. The problem confronting the clinician is to determine when the fungus is really the responsible pathogenic agent in a given case.

Von Graffenried [2] is credited as the first to prove the pathogenic effect on human skin of Monilia derived from interdigital lesions. Subsequently the reproduction of identical lesions on normal skin by inoculation of yeastlike organisms obtained from existing lesions was reported by Greenbaum and Klauder.[3] Stäheli,[4] White [5] and Kingery and Thienes [6] produced acute inflammation of human nail folds by

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1. Benham, R. W., and Hopkins, A. M.: Yeast-Like Fungi Found on the Skin and in Intestines of Normal Subjects, Arch. Dermat. & Syph. **28**:532 (Oct.) 1933.

2. von Graffenried, C.: Beitrag zur Frage der mykotischen Dyshidrosis (Kaufmann-Wolf), Dermat. Wchnschr. **6**:361 (May 25) 1918.

3. Greenbaum, S. S., and Klauder, J. V.: Yeast Infections of the Skin, Arch. Dermat. & Syph. **5**:332 (March) 1922.

4. Stäheli, cited by Shelmire, B.: Thrush Infections of Skin, Arch. Dermat. & Syph. **12**:789 (Dec.) 1925.

5. White, C.: Superficial Yeast Infections of the Glabrous Skin, Arch. Dermat. & Syph. **18**:429 (Sept.) 1928.

6. Kingery, L. B., and Thienes, O. H.: Mycotic Paronychia and Dermatitis, Arch. Dermat. & Syph. **11**:186 (Feb.) 1925.

implanting Monilia albicans isolated from cases of paronychia. More recently Finnerud [7] grew organisms of Cryptococcus and Monilia in pure culture from 77 of 100 cases of perlèche occurring in an orphanage and reproduced a clinically identical disease in 9 out of 10 cases by inoculation of these cultures, repeatedly recovering the organisms in pure culture from such experimentally induced lesions. Dowling [8] produced pathologic effects between the digits with M. albicans but failed to duplicate the typical erosion and concluded that ideal natural conditions could not be copied. But he did succeed in duplicating a vesicular and scaly eruption by inoculating normal skin with monilias cultured from identical lesions on the palms. Freund [9] studied a form of perlèche occurring mainly in women over 40. He based its monilial causation on the following five factors: (1) the demonstration of Monilia in the fresh preparation, (2) the culture of Monilia from scrapings, (3) the coexistence of other monilial dermatoses (interdigital and submammary), (4) the reproduction of lesions by inoculation of normal skin with pure cultures and (5) the effect of tincture of iodine on the lesions.

The case of moniliasis we wish to add to those already reported in the literature is interesting because of the generalized areas of involvement, the chronicity of the disorder and the experimental proof of pathogenicity of Monilia.

REPORT OF CASE

S. S., a white woman aged 41, presented herself at the New York University dermatologic clinic on Aug. 5, 1940. In 1935 she noticed a vaginal discharge, which was soon followed by an eruption about the genitalia and in the groins. In 1936 the skin around the nail of the left index finger became inflamed and swollen and oozed pus. In 1938 the patient became pregnant, and in the fifth month of her pregnancy an eruption appeared on the abdomen, in the folds of the breast and at the angles of the mouth. After birth of the child, the eruption on the abdomen and breasts cleared, but that at the angles of the mouth persisted. In 1939, the right thumb and left ring finger became affected in the same way as the left index finger, and there was involvement of the nails of both great toes. There was also an eruption on the scalp and behind the ears. In 1940 she underwent an operation involving the internal genitalia, and this aggravated the eruption wherever it existed on the body. In August of that year both axillas became involved for the first time.

The dermatosis was generalized and involved the scalp, angles of the mouth, axillas, mammary folds, abdomen, external genitalia and groins. The right thumb,

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7. Finnerud, C. W.: Perlèche: Clinical and Etiologic Study of One Hundred Cases, Arch. Dermat. & Syph. **20**:454 (Oct.) 1929.

8. Dowling, G. B.: The Pathogenicity of Monilia and Other Yeast-Like Fungi, Brit. J. Dermat. **42**:562, 1930.

9. Freund, H.: Ueber eine klinisch und ätiologisch charakterisierte Form von Perlèche bei Erwachsenen, 'Interlabialmykose' und ihre symptomatische Bedeutung, Arch. f. Dermat. u. Syph. **164**:614, 1931.

left index and ring fingers, toe webs and great toe nails were also affected. The parts affected showed erythema, scaling, pinhead-sized to pea-sized closely aggregated papules, partly eroded and oozing, resembling the moist papules of syphilis. The coalescence of these lesions produced large eroded moist surfaces in the axillas, mammary folds, about the genitalia and in the groins. Some lesions on the scalp resembled psoriasis. The affected fingers showed a decided paronychia, and the nails were discolored, lusterless, dull and broken off. The great toe nails showed similar changes, but there was no associated paronychia. The toe webs were scaly and macerated. A few weeks after her first visit to the clinic, an interdigital erosion appeared in the web between the right middle and ring fingers. The clinical picture suggested a generalized moniliasis.

MYCOLOGIC EXAMINATION

Specimens for mycologic examination were taken from the following sites: (1) finger nails, (2) interdigital erosion, (3) right axilla, (4) left great toe nail, (5) right great toe nail, (6) toe webs, (7) scalp, (8) tongue, (9) angles of the mouth, (10) mammary folds, (11) groins, (12) vagina and (13) stools. The scrapings from the finger nails showed fungi in potassium hydroxide preparation, but only a few mycelial filaments were seen and no spores were found. A positive identification of Monilia could not be made from this preparation. In the material from the interdigital erosion there were a network of filaments and clusters of yeastlike budding spores characteristic of Monilia. All other specimens were negative for fungi on microscopic examination (one must consider the possibility that some of these patches might be "moniliids"). Cultures with a gross and microscopic appearance of M. albicans were obtained from the following lesions: (1) interdigital erosion, (2) right axilla, (3) angles of the mouth, (4) breasts, (5) vagina and (6) left great toe nail. The primary colonies grown on dextrose-peptone-agar medium were not identical, and we divided them into two types, A and B (fig. 1). Type A was isolated from the left great toe nail, angles of the mouth and vagina and type B from the interdigital erosion and breasts. From the right axilla colonies of both types were isolated. Cultures of type A were more characteristic for M. albicans. They were yeastlike and creamy white, with a moist and shiny surface and a flat or slightly elevated center which was honeycombed or covered with fine convolutions. The periphery was smooth with superficial radial furrows. There was a deep submerged growth and a corona of fine radiating mycelial filaments, visible on transillumination. Culture mounts fixed and stained in lactophenol blue showed mycelial filaments, roundish yeastlike budding spores and chlamydospores. The filaments were well formed, with cross walls dividing them into elongated cylindric segments. The yeast-

like spores, present in great number, were formed laterally and terminally on the filaments. In the old colonies they formed large spherical clusters attached to the filaments at intervals, especially near the junctions of two mycelial segments. The chlamydospores were few in young cultures but numerous in old ones. They were two to three times as large as the ordinary spores and globular or ovoid, with a heavy double-contoured membrane (figs. 2 and 3).

Fig. 1.—Cultures on dextrose-peptone-agar: left, from the left great toe (type A); right, from the right axilla (type B).

The cultures of type B differed from those of type A in that they were more elevated, with a mass of heaped-up convolutions, and of a darker brownish color; otherwise in gross appearance they were similar to cultures of type A. Microscopically they showed a great number of the chlamydospores even in young colonies.

The differences noted between the cultures of both types were not stable. Cultures of one type produced transfers with the gross and microscopic features of the other type. The colonies showed a decided polymorphism, more or less elevated centers, finer or coarser convolutions, more or less honeycombed surface and lighter or darker color.

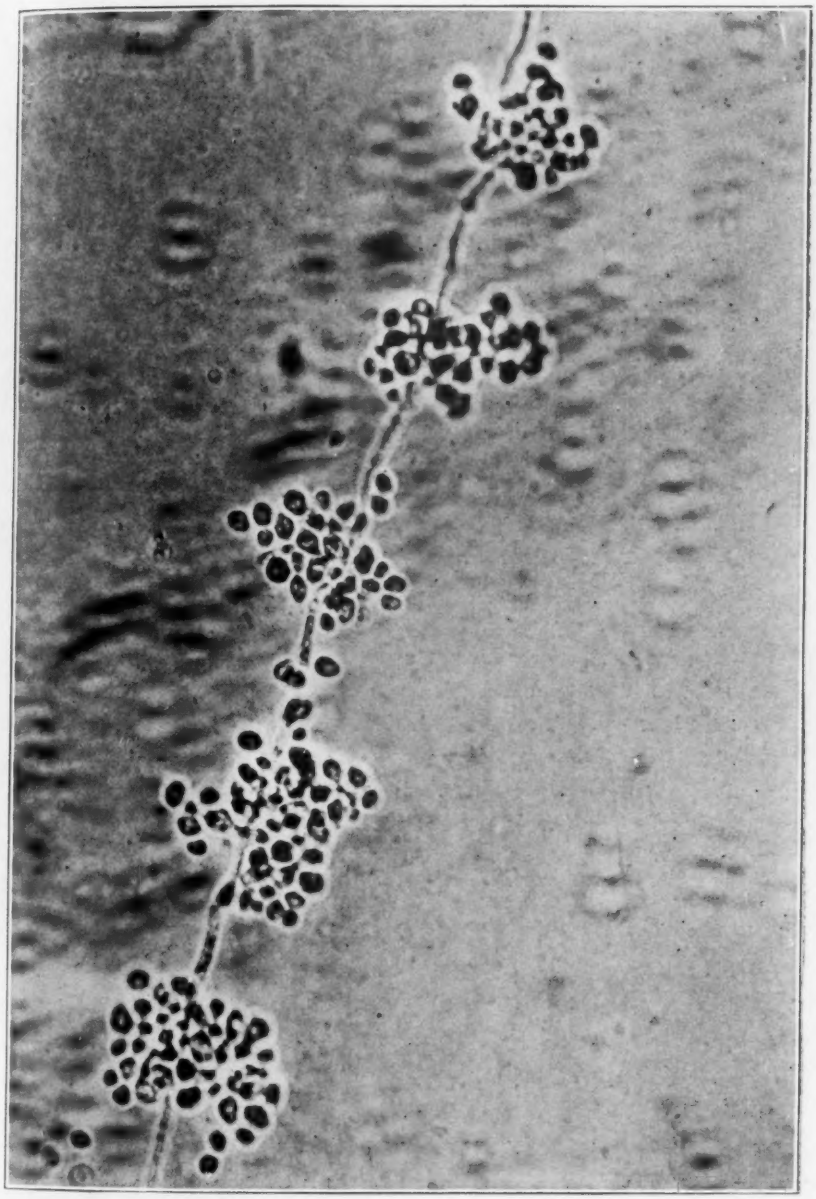

Fig. 2.—Culture mount in lactophenol blue from a culture of type A, showing mycelium with spherical clusters of yeastlike budding spores (× 750).

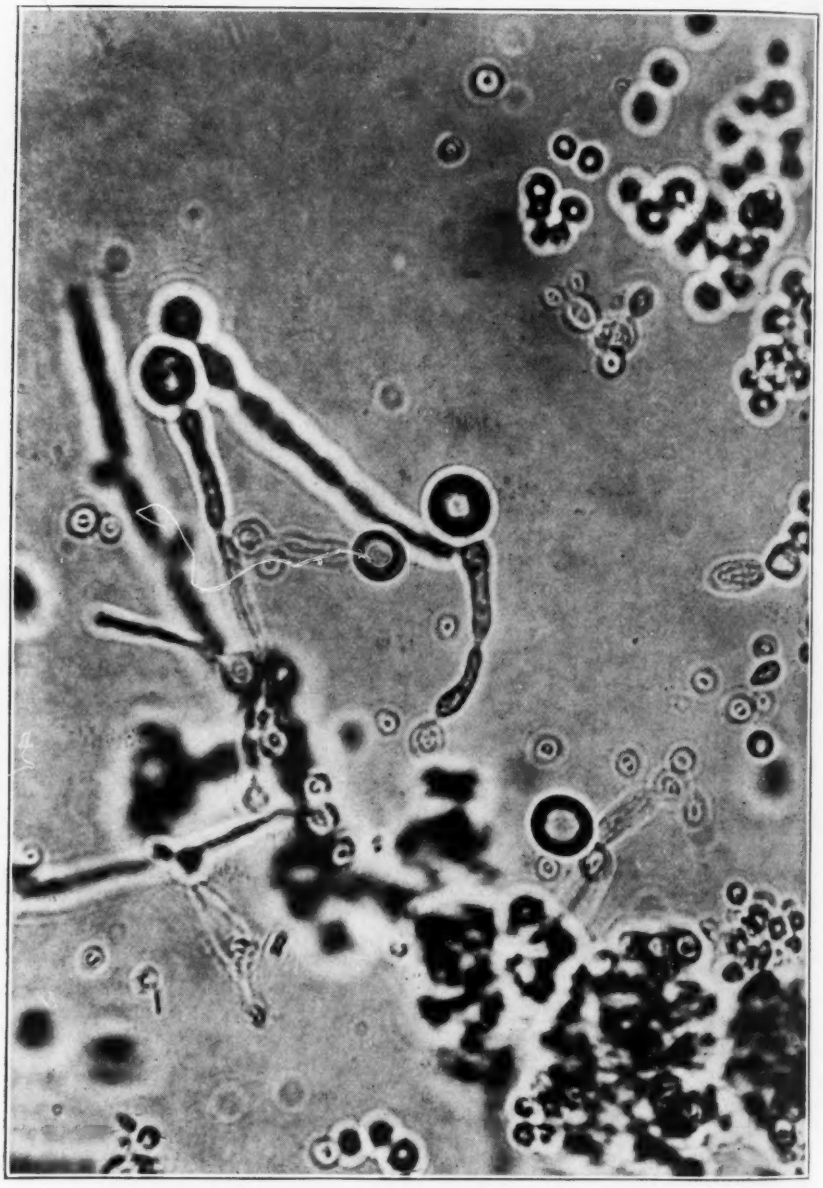

Fig. 3.—Same culture as in figure 2 (× 1,000), showing mycelium, yeastlike spores and chlamydospores. Culture mount in lactophenol blue. The protoplasm is stained; the membrane is colorless.

The microscopic appearance, especially the number of the spherical clusters of spores and of the chlamydospores, also varied in the transfers of the same strain. We believe that all cultures studied could be classified as M. albicans.

EXPERIMENTAL AUTOINOCULATION

With the patient's consent we made inoculations on her left arm and in the intergluteal fold with the material taken from the culture

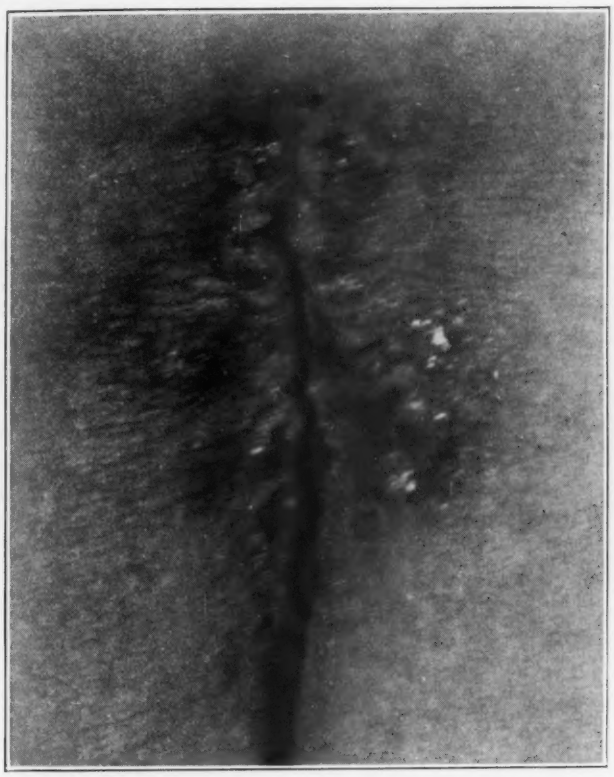

Fig. 4.—Area of experimental inoculation in the intergluteal fold.

isolated from the interdigital erosion (type B). A loopful of the growth was rubbed into a slightly abraded area of skin and covered with cellophane and adhesive plaster. In forty-eight hours the site of the inoculation in the intergluteal fold was a patch of follicular vesicles and pustules on an erythematous and edematous base. In a few days it became a plaque with moist and eroded papules similar to the lesions present in the groins (fig. 4). The inoculation on the left arm gave less noticeable results; several erythematous papules developed, but they

disappeared in a few days without any treatment, while the inoculation patch in the intergluteal fold persisted for several weeks. This could be explained by the fact that the moist area in the intergluteal fold would be a better culture medium.

Microscopic examination of the scrapings taken from the inoculation lesion in the intergluteal fold showed filaments and yeastlike spores characteristic of Monilia. Cultures made from the same material produced colonies identical with the one used for inoculation. The pathogenicity of this strain for the human skin was therefore proved experimentally, at least as far as this patient was concerned.

SUMMARY AND CONCLUSIONS

Several successful autoinoculations proving the pathogenicity of Monilia and other yeastlike fungi in producing eruptions are cited from the literature.

A case is reported in which the clinical diagnosis of generalized moniliasis was proved by the reproduction of similar lesions by autoinoculation and the recovery of the responsible fungus in pure culture.

Any generalized eruption having features similar to the case herein described deserves study from the point of view of monilial infection.

The responsibility of Monilia and other yeastlike fungi as the etiologic agents in any given case needs to be proved, because these fungi may vegetate harmlessly on human skin.

50 Park Avenue.

55 West Forty-Second Street.

TRICHOPHYTON PURPUREUM (BANG) AND TRICHOPHYTON GYPSEUM (BODIN)

DIFFERENTIATION IN CULTURE

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Investigators from a number of dermatologic laboratories in this country and elsewhere have observed, from time to time, cutaneous lesions with particular physical characteristics that constitute a special clinical type of ringworm. One such clinical picture was reported by Lewis, Montgomery and Hopper,[1] in which the specific fungus was isolated and successfully grown in culture. The fungus associated with this disease syndrome they recognized as Trichophyton purpureum (Bang). Another clinical picture of ringworm, exhibiting several types of physical characteristics in this disease syndrome, has been observed by Dowding and Orr [2] as being due to the fungus designated as Trichophyton gypseum (Bodin). While these two disease pictures may sometimes be readily separated in a clinical diagnosis, the separation cannot always be made with certainty. Often the same fungus may cause several different types of lesions, or the same kind of lesion may be caused by different fungi.

In an account of the microscopic appearance of T. purpureum in scrapings from cutaneous lesions, Lewis, Montgomery and Hopper [1] reported that there is nothing characteristic in the appearance of the fungus in the scales, that the amount of the fungus material is sparse and that the mycelium is of approximately the same size as that of T. gypseum, approximately 3 or 4 microns in diameter. In a study of ringworm of the nails, Hodges [3] stated that he was unable to establish any correlation between the appearance of the fungus found in

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1. Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **37**:823-839 (May) 1938.

2. Dowding, E. S., and Orr, H.: Three Clinical Types of Ringworm Due to Trichophyton Gypseum, Brit. J. Dermat. **49**:298-307 (July) 1937.

3. Hodges, R. S.: Ringworm of the Nails: A Preliminary Report of Sixteen Cases of Onychomycosis, Arch. Dermat. & Syph. **4**:1-26 (July) 1921.

the nail parings and the three groups of cultures obtained, namely, types A and B (T. purpureum) and type C (T. gypseum).

Lewis and Hopper,[4] studying the variations in cultural characteristics of five strains of T. purpureum on three closely related culture mediums, reported that there were no consistent differences due to the mediums; the character of the surface growth remained unchanged on the three mediums. Reporting on T. gypseum, Dowding and Orr [2] claimed that this fungus is difficult to determine in culture because strains isolated from different patients often vary one from another and that any individual strain frequently varies with age.

The differentiation of T. purpureum and T. gypseum is frequently made in part on the appearance of the structures found in the microscopic culture mount. However, in the absence of spiral formation and the differentiating fuseaux, which are often difficult to obtain, the microscopic mounts may be indistinguishable. The chief differences noted in the report of Hodges [3] were that for type A, namely T. purpureum, the microscopic mount showed conidiophores, both simple and branched, bearing piriform conidia and pluriseptate fuseaux of characteristic slender form, while for type C, namely T. gypseum, the microscopic mount showed conidiophores, frequently in clusters, bearing piriform, nearly oval conidia, rather short fuseaux and numerous characteristic spirals.

Since the first published reports of T. purpureum [5] this microorganism has been reported as a common cause of onychomycosis [3] and as a frequent cause of eczema marginatum.[6] It is reported as being present in the southern part of the United States,[7] while the same organism causes 6 per cent of dermatophytosis in Puerto Rico.[8] Recently 4 cases of extensive lichenified dermatitis caused by T. rubrum (purpureum) were reported from Boston.[9]

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4. Lewis, G. M., and Hopper, M. E.: Cultural Variations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **41**:895-903 (May) 1940.

5. Bang, H.: Sur une trichophytée cutanée à grands cercles, causée par un dermatophyte nouveau (Trichophyton purpureum Bang), Ann. de dermat. et syph. **1**:225-238, 1910. Castellani, A.: Observations of a New Species of Epidermophyton Found in Tinea Cruris, Brit. J. Dermat. **22**:147-150, 1910.

6. Ota, M.: Contributions to the Study of Trichophyton Purpureum Bang, Trichophyton Interdigitale Priestly and Trichophyton "B" Hodges, Arch. Dermat. & Syph. **5**:693-715 (June) 1922.

7. Weidman, F. D.: Laboratory Aspects of Epidermophytosis, Arch. Dermat. & Syph. **15**:415-450 (April) 1927.

8. Carrión, A. L.: Preliminary Report on the Fungus Causing Epidermophytosis of the General Surface of the Skin in Porto Rico, Porto Rico J. Pub. Health & Trop. Med. **5**:40-44 (Sept.) 1929.

9. Swartz, J. H., and Conant, N. F.: Extensive Lichenified Eruption Caused by Trichophyton Rubrum, Arch. Dermat. & Syph. **42**:614-624 (Oct.) 1940.

T. gypseum with its many variants has been reported by Legge, Bonar and Templeton [10] as one of the most prevalent dermatophytes of ringworm of the foot of university students in California. Kauffmann-Wolf [11] found 68 per cent infections with T. gypseum in an examination of 25 cases of ringworm of the foot, Schmidt [12] found 77 per cent infections with the Kauffmann-Wolf fungus, namely T. gypseum, in examining 732 patients with ringworm of the hand and foot. Mitchell [13] found T. gypseum in 33 per cent of the 121 patients that he examined, and in a study made at Edmonton, Alberta, Canada, on 200 patients suffering from ringworm, Dowding and Orr [2] reported that T. gypseum was responsible for 67 per cent of the infections.

Clinically in the separation of lesions caused by T. purpureum from lesions caused by T. gypseum there seems to be no generally accepted differentiation. Furthermore these two fungi are not separable at all by the appearance of the organism in the direct microscopic mount, and as yet the differentiation on a purely cultural basis is still rather unsatisfactory. For these reasons it was thought advisable to attempt by further cultural means to render the separation of T. purpureum and T. gypseum somewhat more definite.

LABORATORY STUDY

In this study interest was primarily centered in the cultural and differentiable characteristics of T. purpureum and T. gypseum. When newly isolated from cutaneous lesions and grown on honey agar or on sabouraud maltose and dextrose agars, it is frequently difficult to distinguish a culture of T. purpureum from one of T. gypseum with any degree of certainty macroscopically. In many cases only after a prolonged study of the microscopic culture mount under favorable conditions can these two dermatophytes be definitely separated. A laboratory study, therefore, was made in an attempt to separate the two fungi readily by the use of different culture mediums. Various strains of T. purpureum (twenty in all) and T. gypseum (fifteen strains), some newly isolated and others taken from old stock cultures, were used. It was possible to demonstrate that the strains of a particular species were fairly uniform in their growth appearance on any one particular medium

10. Legge, R. T.; Bonar, L., and Templeton, H. J.: Ringworm of the Feet: Preliminary Report, J. A. M. A. **92**:1507-1508 (May 4) 1929.

11. Kauffmann-Wolf, M.: Ueber Pilzerkrankungen der Hände und Füsse, Dermat. Ztschr. **21**:385-396, 1914.

12. Schmidt, B. W.: Zur Pathogenese der Epidermophytien und Trichophytien der Hände und Füsse, Arch. f. Dermat. u. Syph. **169**:259-294, 1933.

13. Mitchell, J. H.: Further Studies on Ringworm of the Hands and Feet, Arch. Dermat. & Syph. **5**:174-197 (Feb.) 1922.

but that the strain varied greatly in its growth habit when it was cultured on a number of different mediums. Seven different culture mediums were used in this differential study.

A. *Cultural Features.*—The seven agar mediums, with their several ingredients, which were used in the present comparative study and on which the conclusions of this paper are based are itemized as follows:

Medium 1. Wort

Maltose	12.75 Gm.
Malt extract	15 Gm.
Dextrin	2.75 Gm.
Glycerin	2.35 Gm.
Dipotassium hydrogen phosphate	1 Gm.
Ammonium chloride	1 Gm.
Peptone	0.78 Gm.
Agar	15 Gm.
Water	1,000 cc.

Medium 2. Honey

Honey	60 Gm.
Peptone	10 Gm.
Agar	20 Gm.
Water	1,000 cc.

Medium 3. Potato

Potato	200 Gm.
Dextrose	20 Gm.
Agar	30 Gm.
Water	1,000 cc.

Medium 4. Currie-Oleic

Dextrose	50 Gm.
Ammonium nitrate	2.5 Gm.
Potassium dihydrogen phosphate	1 Gm.
Magnesium sulfate	0.25 Gm.
Agar	20 Gm.
Water	1,000 cc.

Plus 1 per cent of oleic acid

Medium 5. Corn Meal

Corn meal	40 Gm.
Agar	15 Gm.
Water	1,000 cc.

Medium 6. Maltose

Maltose	40 Gm.
Peptone	10 Gm.
Agar	20 Gm.
Water	1,000 cc.

Medium 7. Currie

Medium 4 minus the oleic acid

1. T. purpureum: The young colony of T. purpureum at first is pure white, fluffy and hemispherical, lacking coloration or pigmentation. The surface of the mature colony may be flat and smooth, with compact fluffy growth and pinkish circular bands above and dark rose-purple pigment on the under surface, or the surface may be granular, powdery and pinkish purple above and dark rose-purple on the under surface. The dark red-purple pigment which forms at the base of the colony is a fairly constant characteristic on some of the mediums. Lewis and

Hopper [14] in a recent publication stated that the presence of certain monosaccharides, such as dextrose, levulose and mannose, permit the formation of pigment by T. purpureum and Microsporum lanosum. Under filtered ultraviolet rays the young colony is a bright light blue, but the periphery alone presents a light blue border in the older colony. The appearance of the colony at maturity, determined by the medium on which the fungus is cultured, is as follows:

(1) Wort agar: The colony presents a downy, compact, smooth surface in the center with a loose, flat, moist appearance toward the periphery (fig. 1, *B*1). It is somewhat grayish above, and a dull dark brown pigment forms below. Growth is rather slow.

(2) Honey agar: The colony has a smooth, compact, powdery to downy surface with shallow grooves radiating from the center (fig. 1, *B*2). It is pale

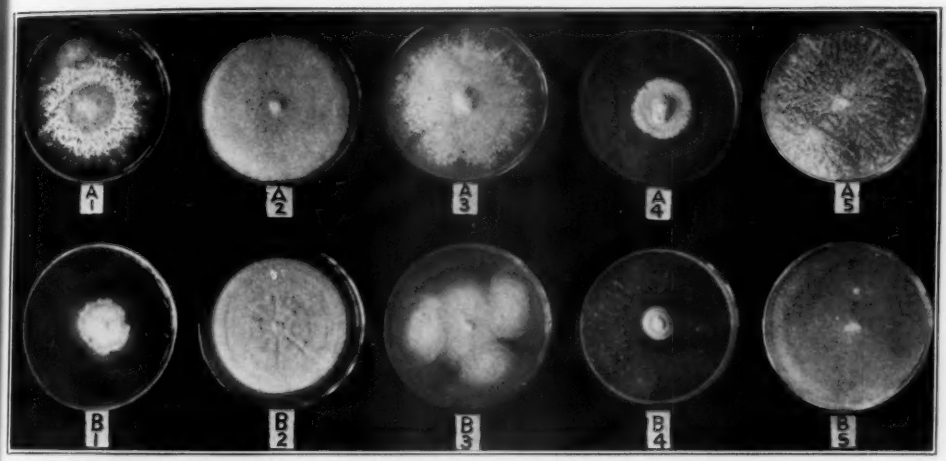

Fig. 1.—Appearance of T. gypseum (*A*) and T. purpureum (*B*) after thirty days on the following mediums: (1) wort, (2) honey, (3) potato, 4) Currie-oleic and (5) corn meal.

tan above, and a dull brown to dark purple pigment forms below. Growth is rapid.

(3) Potato agar: A characteristic colony develops, forming a smooth, compact, downy surface (fig. 1, *B*3; fig. 2, *B*3). The color, which sometimes appears in circular bands, is pinkish violet above. The pigment that forms below often occurs in circular bands and is reddish purple. Growth is rapid.

(4) Currie-oleic agar: The colony is slow of growth and forms a pasty, corrugated surface that is grayish white above; there is no noticeable development of pigment below (fig. 1, *B*4).

14. Lewis, G. M., and Hopper, M. E.: Pigment Production by Fungi, Arch. Dermat. & Syph. **44**:453-460 (Sept.) 1941.

(5) Corn meal agar: The colony is rather slow of growth and forms a smooth, moist, granular surface (fig. 1, *B5*). It is grayish white above, and there is no distinct pigment formation below.

(6) Maltose agar: The colony has a smooth, compact, downy surface, often with deep radial grooves and sometimes surrounded by a moist peripheral border

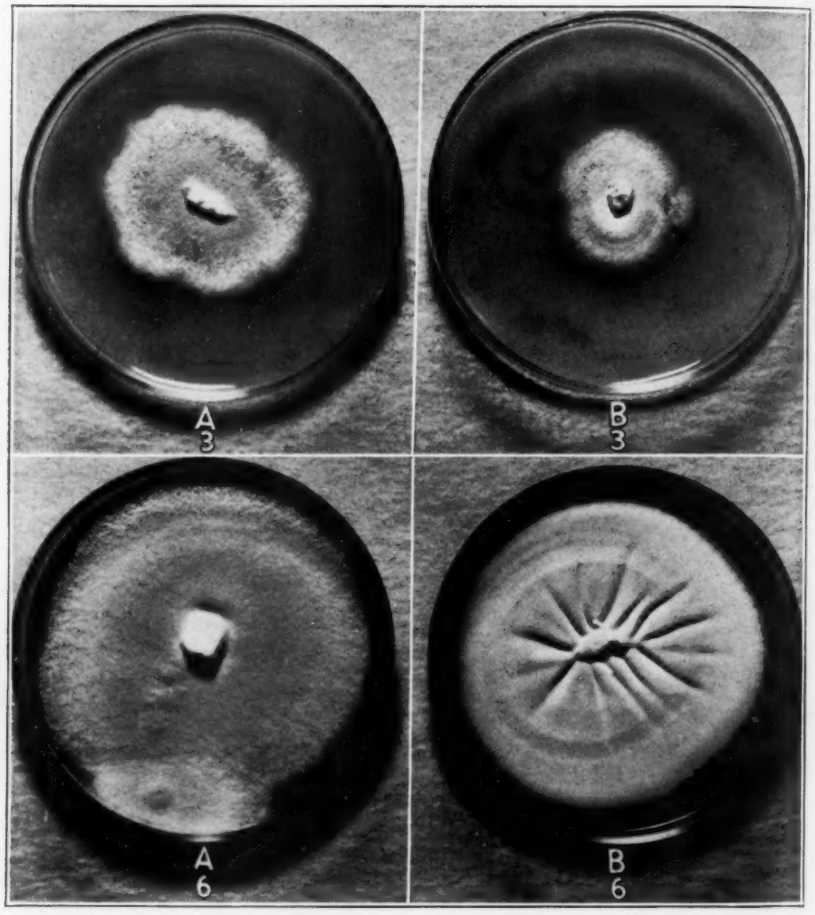

Fig. 2.—Appearance of T. gypseum (*A*) and T. purpureum (*B*) on potato agar (3) after fifteen days and on maltose agar (6) after thirty days.

(fig. 2, *B6*). It is grayish white above, and dull dark purple pigment forms below. Growth is rapid.

(7) Currie agar: The surface of the colony is compact, raised and powdery, often with circular or irregular folds. A yellowish cream color develops above and reddish brown pigment below. Growth is slow.

2. T. Gypseum: The young colony of T. gypseum is pure white at first with a flat, compact surface growth and without coloration or

pigmentation of any kind. The upper surface of the mature colony may be flat, smooth, powdery in texture and cream-yellow to yellow-tan in color, with a dull salmon-colored pigment in the lower surface, or the upper surface of the colony may be flat, mealy, dotted with tufts of fluffy white growth and cream-yellow to yellow-tan over the smooth areas, with a dull salmon-colored pigment on the under surface. The dull salmon-colored pigment which forms at the base of the colony is a common characteristic on many of the mediums. Under filtered ultraviolet rays the central part of the colony is bright, light purple-violet and the periphery is yellowish brown to lilac colored. The appearance of the colony at maturity is determined by the medium on which the fungus is cultured:

(1) Wort agar: The colony has a loose powdery surface with a cobwebby center and a coarse mealy periphery (fig. 1, *A*1). It is grayish cream above, and dull reddish brown pigment forms below. Growth is rather slow.

(2) Honey agar: The colony presents a smooth, compact surface with a powdery tan center and fluffy white periphery above. A dull yellowish brown pigment forms below (fig. 1, *A*2). Growth is rapid.

(3) Potato agar: A characteristic colony develops, marked by a close, granular, mealy appearance (fig. 1, *A*3; fig. 2, *A*3). The upper surface of the colony has a yellowish cream center and a feathery white periphery. The lower surface forms dull salmon-colored pigment toward the center and yellowish cream pigment toward the periphery. Growth is rapid.

(4) Currie-oleic agar: The colony is slow of growth and forms a dry, pasty and honeycombed surface that is grayish white above; a pale salmon-colored pigment forms below (fig. 1, *A*4).

(5) Corn meal agar: The colony is rather rapid in growth and forms a loose, netted and dotted granular surface (fig. 1, *A*5). The colony is grayish white above, and there is no noticeable formation of pigment below.

(6) Maltose agar: The colony has a flat, smooth, compact, powdery surface (fig. 2, *A*6). Above it is grayish tan in the center and grayish white toward the periphery; below a dull dark brown pigment forms in the center surrounded by a pale salmon-colored periphery. Growth is rapid.

(7) Currie agar: The surface of the colony is coarse, granular and often irregularly formed radially. A grayish cream color develops above and yellowish orange pigment below. Branched, rhizomorphic-like structures sometimes develop from the periphery of the colony and lie embedded in the medium. Growth is slow.

3. Comment on Cultural Features: While the several strains of a species often showed many recognizable variations on the same culture medium, the changes observed when the species was cultured on different mediums were pronounced. These changes were shown in size of colony, surface appearance, color formation and extent and intensity of pigment development.

In cultures of T. purpureum there were giant colonies on mediums 2, 3 and 6, dwarf colonies on 1, 4 and 7, powdery colonies on 2 and 6,

compact colonies on 1, 2, 3 and 6, pasty colonies on medium 4 and orange to brown pigmented colonies on 7. The pinkish color was most evident on medium 3 and least evident on mediums 1, 4, and 5. The rose-purple pigment was distinct on the lower surface of mediums 2 and 6 and particularly striking on the lower surface of medium 3. Under filtered ultraviolet rays the young colonies of T. purpureum on mediums 1, 2, 3 and 6 were a clear light blue.

In cultures of T. gypseum there were giant colonies on mediums 2, 3 and 6, dwarf colonies on 1, 4 and 7, powdery colonies on mediums 1, 2, 3 and 6, compact colonies on 2 and 6, pasty colonies on medium 4 and rhizomorphic-like colonies on 7. The yellow-tan color was most pronounced on medium 3 and least pronounced on mediums 1, 4 and 5. The dull salmon-colored pigment was distinct on the lower surface of mediums 2 and 6 and striking on the lower surface of medium 3. Under filtered ultraviolet rays the young colony on mediums 1, 2, 3 and 6 was a clear purple-violet.

It seems probable that little advantage may be gained in the way of a clearer differentiation between these two fungi by further experimentation with new culture mediums, unless the particular effect of each individual ingredient of the medium is analyzed separately. For instance, Currie agar, corn meal agar and Currie-oleic agar showed no single character or group of characteristics that might possibly serve as a basis for identification of T. purpureum or for differentiation from T. gypseum. The colony formed on wort agar had definite characteristics, but they were not clearly differentiable from those of T. gypseum. The three mediums represented by honey, maltose and potato agars exhibited distinctive characteristics that were closely parallel in all three cultures. In this instance, the rapidity of growth, the surface appearance, the color of the colony above and the color of the pigment elaborated below all were similar for those three mediums. On potato agar, however, those distinguishing characteristics were more clearly defined in the regularity of occurrence than on honey and maltose. Those three mediums served best in the differentiation between T. purpureum and T. gypseum, and of the three potato agar cultures showed the most contrasting characteristics. On potato medium the deep reddish purple pigment is striking for T. purpureum and the dull salmon-colored pigment is likewise outstanding for T. gypseum. While the particular group of characters by which the trained laboratory observer learns to recognize these organisms frequently varies in cultures grown on honey and maltose, it is also true that departure from the normal type sometimes occurs in the appearance of new strains of both organisms when grown on potato agar. In the main, however, it seems clear that the characters of T. purpureum and T. gypseum are more constant, and there is less variation shown in newly isolated strains of these fungi when

they are cultured on potato-medium than when cultured on certain other mediums (fig. 1, *A* 3 and *B* 3).

One strain of T. purpureum, recently isolated and grown in the laboratory on a honey agar medium, formed three distinct saltations as sectors in a colony with typical rose-purple pigment. One sector was white, one yellow and one tan. Contrary to the results obtained by other workers, however, I found that all three of these saltations produced a typical rose-purple pigmented colony when cultured on a potato agar medium. The transfers to potato agar were made in mass, and the peculiar finding was not continued. It is noted here merely because it differs radically from the findings of other investigators, in which the saltation on transfer retained its changed characteristics.

B. Microscopic Culture Mount.—1. T. Purpureum: Microconidia *en grappes,* thyrsi sporiferae and chlamydospores were the three structures normally present on all seven mediums. Fine mycelium with filaments of an undulant nature, 2 to 3.5 microns in diameter, was common. Macroconidia (fuseaux) were infrequent or absent from all mediums. When searched for, they were occasionally found on wort agar. Macroconidia can be produced readily, however, in beef bouillon (Sabouraud), in serum (Spring), in ascitic fluid (Hopkins), on polished rice (Swartz and Conant) and on natural mediums such as grains of barley, wheat and rye (Langeron and Milochevitch).

The microconidia are elongate-piriform in shape, average 3 by 5 microns in size and are frequently longer than those of T. gypseum. The macroconidia average 6 by 60 microns in size and are long and slender with parallel sides. The distal end is rounded, and the base is broad. The macroconidia are faintly several times (two to ten) septate, and the walls are thin and smooth. This slender spore, with regular shape and parallel sides, is probably unique among the Trichophyta and appears in striking contrast to the irregularly shaped, somewhat piriform macroconidia of T. gypseum.

2. T. gypseum: Five structures were frequently present in mounts made from all seven culture mediums. These structures were microconidia *en grappes,* thyrsi sporiferae, chlamydospores, racquet mycelium and spirals. The mycelium was generally coarse and somewhat irregular, often measuring 3 to 4.5 microns in diameter. Spirals formed abundantly on potato and corn meal agars. Macroconidia (fuseaux) were infrequent but formed plentifully in scattered patches and in circular bands on wort agar.

The microconidia are oval-piriform in shape and average 2.5 by 3.5 microns in size. The macroconidia average 8 by 45 microns in size, are clavate or piriform to cylindric in shape, have smooth, thin walls and are rounded at the distal end and constricted at the septation

points. The cross septums are relatively few (four to eight) but distinct. The macroconidia are shorter, thicker and less regular than those of T. purpureum.

SUMMARY

1. Of the seven culture mediums used in this investigation, the potato medium showed the most definitive differences in a macroscopic separation of T. purpureum and T. gypseum.

2. The downy-appearing surface with a white or pinkish color above and the constancy of a dark reddish purple pigment in the lower surface of the mature colony was characteristic for T. purpureum.

3. The powdery appearance of the surface with a white to cream color above and the uniformity of a dull salmon-colored pigment in the lower surface of the mature colony was typical of T. gypseum.

4. Under filtered ultraviolet rays the young culture of T. purpureum exhibited a clear, light blue fluorescence and T. gypseum showed a clear, purple-violet fluorescence.

5. In microscopic culture mounts the strains of T. purpureum invariably lacked spiral elements and formed microconidia of the large, elongate-piriform type. T. gypseum always produced spirals in abundance and microconidia of the small, oval-piriform type.

6. When observed the macroconidia of T. purpureum were unquestionably distinctive, relatively long, slender, cylindric, septate spores with parallel sides. The macroconidia of T. gypseum were short, thick, piriform, septate spores with irregularly constricted sides.

UNUSUAL SITES OF LESIONS IN PELLAGRA

GANGRENE OF THE TOE IN ONE CASE

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The dermatitis seen in pellagra usually affects the dorsal surfaces of the hands and wrists, the neck and parts of the face. In European countries the feet and ankles are frequently affected, but in the United States these areas usually escape. Wood [1] cited the following figures for the distribution of cutaneous lesions in pellagra: In 182 cases, or 95.3 per cent, lesions were seen on the backs of the hands. In 36 cases, or 19 per cent, lesions appeared on the neck. In 4 cases, or 2.1 per cent, lesions were noticed on the feet only (all children). Merk [2] gave these figures: In 1,679 cases, or 77 per cent, lesions occurred on the backs of the hands. In 282 cases, or 13 per cent, lesions were seen on the backs of the hands and neck. In 164 cases, or 7.5 per cent, lesions appeared on the neck. In 53 cases, or 2.4 per cent, lesions appeared on other parts of the body.

We have encountered many cases of pellagra at Bellevue Hospital, but this is the first time we noticed lesions under the breasts, in the intergluteal region, around the vulva and on the inner aspects of the thighs. Wood and Merk did not mention any of these sites in their surveys. It is for this reason that we wish to report the following cases.

REPORT OF CASES

CASE 1.—H. J., a Negress aged 31, was admitted to Bellevue Hospital complaining of soreness of the mouth and tongue. She gave a history of drinking heavily for six months prior to admission. She noticed "moist areas" beneath the breasts and around the genitalia and anus three weeks prior to admission. On admission the patient complained of severe pains in the arms and legs of one week's duration.

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1. Wood, E. J.: A Treatise on Pellagra for the General Practitioner, New York, D. Appleton and Company, 1912, p. 167.

2. Merk, C. B., cited by Wood.[1]

Examination revealed a poorly nourished and depressed Negress. The lips were dry, scaly and fissured. The tongue was swollen, dry and bright red. Beneath the breasts and extending peripherally for 2½ inches (6.3 cm.) were areas of pigmentation, scaling and some exudation (fig. 1). The dorsal surfaces

Fig. 1 (case 1).—Lesions of pellagra beneath breasts.

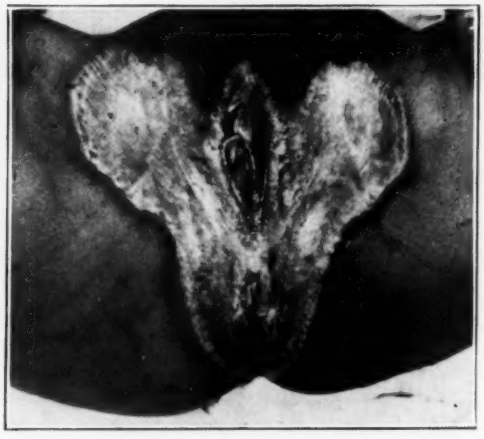

Fig. 2 (case 1).—Lesions of pellagra in the anogenital region.

of the fingers were dry and scaly. Exudation and erythema were seen around the vulva and intergluteal regions (fig. 2), extending peripherally for about 3 inches (7.5 cm.). There were signs of a peripheral neuritis.

The Wassermann reaction of the blood was negative. The urine was normal. A blood count showed a moderate anemia.

The lesions responded rapidly to the administration of nicotinic acid. The peripheral neuritis responded to treatment with thiamine hydrochloride.

CASE 2.—R. J., a Negro aged 28, was admitted to Bellevue Hospital complaining of a rash on the hands and feet of one year's duration. He stated that the eruption would clear up at times but that it had been getting worse for two months prior to admission. He has been a heavy drinker of alcoholic liquor for the past thirteen years. On admission the patient complained of burning and soreness of the mouth, diarrhea, pains in the arms and legs and a "bad smell" from the right big toe. There was no history of injury to the affected toe.

Examination revealed dryness and fissuring of the lips. The tongue was swollen, dry and denuded. The backs of the hands presented areas of pigmentation and scaling. The dorsal surfaces of the feet and toes showed similar patches of pigmentation, depigmentation and scaling. There was a well demarcated area of slough on the medial aspect of the right great toe at its base

Fig. 3 (case 2).—Gangrene at the base of the great toe in a case of pellagra.

(fig. 3). There was no evidence of ascending lymphangitis, nor were there tender femoral nodes. The peripheral pulses were easily palpable with strong pulsations. The temperature was normal. The surgical consultant diagnosed the condition as an infected abrasion of the right great toe with local gangrene on the basis of a pellagrous dermatitis.

The Wassermann reaction of the blood was negative. The red blood cell count was 3,560,000, and the hemoglobin content was 80 per cent. The white blood cell count was 13,200, and the differential count was normal. The urinalysis showed a 2 plus reaction for albumin. A roentgenogram of the right great toe revealed trophic destruction of the distal phalanx of the right great toe and the distal articular end of the proximal phalanx.

The cutaneous lesions responded to the administration of nicotinic acid. Treatment with thiamine hydrochloride relieved the peripheral neuritis. The right great toe was amputated at the metatarsophalangeal joint.

CASE 3.—C. C., a Negress aged 48, was admitted to Bellevue Hospital complaining of severe pains in the anal region of five days' duration. She drank

heavily for three months prior to admission, during which time she lost weight and noticed an eruption on the dorsal surfaces of the hands, around the anus and vulva and beneath the breasts.

Examination revealed a swollen red tongue. The lips were dry and fissured. There were scaling and pigmentation beneath the breasts. The dorsal surfaces of the hands were dry and pigmented, with several areas of scaling. The entire area surrounding the vulva and anus, including the inner aspect of the thighs, presented fissuring and desquamation. A tender external hemorrhoid was felt at the anal margin.

The Wassermann reaction of the blood was negative.

The cutaneous lesions responded rapidly to the administration of nicotinic acid.

SUMMARY

Three cases of pellagra with lesions in unusual sites, the areas beneath the breasts, the intergluteal region, the area around the vulva and the inner aspects of the thighs, are reported.

In 1 case local gangrene of the right great toe on the basis of a pellagrous dermatitis was seen.

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CUTANEOUS FISTULAS OF DENTAL ORIGIN

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Although cutaneous fistulas of dental origin are rather common lesions, information concerning them is not as widespread as one might suppose. Interest in the recent reports of Anderson,[1] Montgomery,[2] Shelton,[3] Eibrink Jansen,[4] Thews[5] and Kohn[6] relative to these lesions, together with the number of cases referred to us as instances of "skin cancers," has led to this report.

Montgomery[2] stated: "Although rarely mentioned in differential diagnosis, the mouth of a fistula may so resemble a cutaneous cancer as to deceive one into treating it as such." He further cited MacKee and Cipollaro,[7] who called attention to the fact that "long continued inflammatory processes not infrequently give rise to cancer."

Some question the degree of malignancy or the possibility of pseudo-epitheliomatous changes in such lesions. Both clinically and histopathologically a cutaneous fistula resembles an epithelioma of the skin. In one of our cases (case 6) the lesion definitely falls into this category by virtue of two conflicting histologic reports. A biopsy of the skin showed "squamous cell carcinoma of differentiated cell type with pearl formation, showing very pronounced inflammatory reaction in the supporting stroma." On the other hand, the tissue adherent to the extracted retained root was described as follows: "Tissue from the mandible showed a marked inflammatory reaction in fibrous connective tissue

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From the State Institute for the Study of Malignant Diseases, Burton T. Simpson, M.D., Director.

Read at a meeting of the Western New York Branch, American Association for Cancer Research, May 12, 1942.

1. Anderson, N. P.: Persistent Sinus Tracts of Dental Origin, Arch. Dermat. & Syph. **35**:1063-1073 (June) 1937.

2. Montgomery, D. W.: Fistulas from Dead Teeth Simulating Dermal Epithelioma, Arch. Dermat. & Syph. **41**:378-379 (Feb.) 1940.

3. Shelton, J. M.: Fistula from Retained Dental Root, Arch. Dermat. & Syph. **42**: 938-939 (Nov.) 1940.

4. Eibrink Jansen, G. A. H.: Cutaneous Fistulas Originating from Infected Teeth, Geneesk. gids **16**:1007-1010 (Sept. 16) 1938.

5. Thews, K.: Unrecognized Fistula, Röntgenpraxis **11**:631 (Nov.) 1939.

6. Kohn, S. I.: Facial Fistulas of Dental Origin, Am. J. Orthodontics **26**: 797-802 (Aug.) 1940.

7. MacKee, G. M., and Cipollaro, A. C.: Cutaneous Cancer and Precancer: A Practical Monograph, New York, American Journal of Cancer, 1937, p. 85.

and muscle with thickening and proliferation of surface mucosa extending downward into inflammatory tissue."

The precursor to such a facial cutaneous lesion is the dental alveolar abscess. This type of abscess is usually associated with nonvital teeth, retained roots and so-called "residual infection" following extraction of pathologic teeth. Some patients with these lesions report having had a so-called "gum boil" previous to the cutaneous lesion.

Anderson [1] stated: "Gravity undoubtedly plays a considerable role in determining the course of the sinus." He also quoted Endelman. "The path of a sinus from an acute alveolar abscess is determined by the location of the involved tooth, the density of the tissues in the region of the abscess, the virulence of the infection, the influence of gravity and finally by the injudicious use of hot poultices." [8]

According to Kohn,[6] who reported 3 cases in children, the mechanism may be acute. He also stated the opinion that such lesions can result from traumatic cysts. Observance of a facial cutaneous lesion having a red nodular shape with purulent discharge in the region of the mandible or maxilla should bring to mind the possibility of dental causation. Shelton [3] emphasized the importance of dental roentgenograms in such cases. He also described the difficulty sometimes encountered in observing the presence of retained roots in edentulous jaws. For this reason it is well to bear in mind that intraoral roentgenograms show more detail of the teeth and associated structures than extraoral films and that it is well to take such films at varying time exposures and at different angles. Injection of radiopaque solutions and exploratory introduction of probes into the suspicious lesions are also valuable diagnostic adjuncts.

It would appear that sufficient diagnostic data can be obtained by clinical and roentgenographic examination so that resort to biopsy except in questionable cases is unnecessary. While Montgomery [2] was cognizant of the esthetic and cosmetic ill effects which might result from biopsy in such cases, he apparently was not entirely against this procedure as a cancer control measure. Cosmetic appreciation in this regard led Galea [9] to devise a "procedure for avoiding umbilication of cutaneous fistulas."

Complete agreement exists among all students of these lesions as to treatment. All advocate extraction and curettement of the offending tooth structure and contiguous infected granulation tissue and abscess.

Herewith are briefly presented 11 cases of cutaneous fistulas of dental origin.

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8. Endelman, J.: Special Dental Pathology, ed. 2, St. Louis, C. V. Mosby Company, 1927, p. 264.

9. Galea, M. G.: Procedure for Avoiding Umbilication of Cutaneous Fistulas of Dental Origin: Squirru Device, Semana méd. **2**:1339-1340 (Dec. 8) 1938.

REPORT OF CASES

CASE 1.—Mrs. L. N., aged 53, had a swelling which appeared about three weeks previous to her admission to the hospital on the left side of the neck. It increased rapidly in size and gradually became hard. It also was becoming sore and painful. There was no bleeding or discharge. Clinical examination revealed a cystic swelling beneath the skin which seemed to fluctuate in the left side of the neck below the angle of the mandible. There was a lower left molar tooth with a gold shell crown present. The tooth was very loose, indicative of considerable loss of alveolar structure, and there appeared to be some pus exuding from the free margin of the gum. Roentgenograms showed a carious devitalized molar with a large area of rarefaction around both roots. Involvement of caries underneath the crown had resulted in the distal root being entirely separated from the rest of the tooth at the root bifurcation. The tooth was extracted and the alveolus curetted, and the patient has remained well for eight years.

CASE 2.—C. S., a girl aged 11 years, had a lump on the lower part of the left cheek. A small lump appeared about eight months previous to her admission to the hospital; this gradually became raised, extended downward on the cheek and also increased in size. About three months later the lesion was opened by her physician, and after that there was a continuous serous and purulent discharge from it. Examination revealed a crusted indurated fistulous opening in the skin of the cheek adjacent to the region of the first molar tooth. Dental examination revealed a carious lower left first molar which was nonvital. Roentgenograms showed a circumscribed rarefied area involving the bone around the root apexes of this tooth. The tooth was extracted and the alveolus curetted. The patient has remained well for three years.

CASE 3.—Mrs. H. D., aged 39, one and a half years previous to admission to the hospital noticed that her chin was sore. Later the skin itched and burned. About two months before she was admitted a definite growth appeared. On admission there were a swelling of the chin and a small fistulous opening in the skin, which was reddened and inflamed. Many carious lower anterior teeth were present. Caries was so advanced that the crowns of some of the teeth had been entirely lost. A biopsy showed infected granulation tissue. Roentgenograms showed rarefied areas around the lower cuspid, the first bicuspid and the second bicuspid. There were also rarefied areas about the retained roots of the incisors. All the lower teeth were extracted, and the lesion healed. It has now been healed for four and a half years.

CASE 4.—Mrs. L. G., aged 38, noticed a reddened slightly raised hardened area on the skin of the right cheek near the chin about twenty days previous to her admission to the hospital. About one week before she was admitted it came to "a head" and discharged some pus. No treatment had been given. On admission there was a fistulous opening in the skin of the right cheek about 1.5 cm. in diameter. There was some fixation of the adjacent tissues. The oral hygiene was poor, and there was a loose molar tooth surrounded by granulation tissue. There was a small palpable node in the right submaxillary region. Histologic examination revealed chronic inflammatory tissue assuming the proportions of a small abscess (fig. 1). Roentgenograms revealed rarefaction of the alveolus of the molar. The tooth was extracted, and the patient has remained well for four years.

CASE 5.—C. K., a woman aged 21, unmarried, had a lesion which began as a reddened swelling in the skin at the angle of the left mandible about three months previous to her admission to the hospital. It had been drained on three

occasions, and the swelling was greatly reduced. There was no pain or soreness, but pus was still draining. Further examination of this region showed a carious molar tooth which appeared to be nonvital. A biopsy showed "infected necrotic tissue from the left jaw." Roentgenograms showed a nonvital lower left molar with slight rarefaction around the apexes. The tooth was extracted and the alveolus curetted. The patient has remained well for three and a half years.

CASE 6.—A. D., a man aged 70, had his lower teeth extracted two years previous to his admission to the hospital. Six months after the extraction a fistula

Fig. 1 (case 4).—Histologic section showing papilloma with chronic inflammatory changes.

developed in the skin of the right cheek, from which some pus escaped. Examination revealed a depressed granular-like fistula on the skin of the face in the region of the lower right first molar tooth. This lesion was surgically removed and examined histologically. The pathologist reported that the section showed a "squamous cell carcinoma of differentiated cell type with pearl formation, showing very pronounced inflammatory reaction in the supporting stroma" (fig. 3). Roentgenograms showed a retained root in the region of the lower right first molar with a rarefied area. The retained root was removed together with considerable granulomatous-appearing tissue. A section was made of this, and the

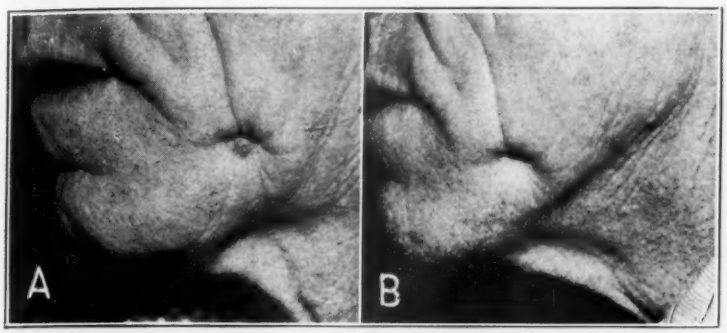

Fig. 2 (case 6).—*A*, granuloma from a fistula associated with the lower left second molar, which was nonvital and infected. *B*, healed lesion with depressed scar.

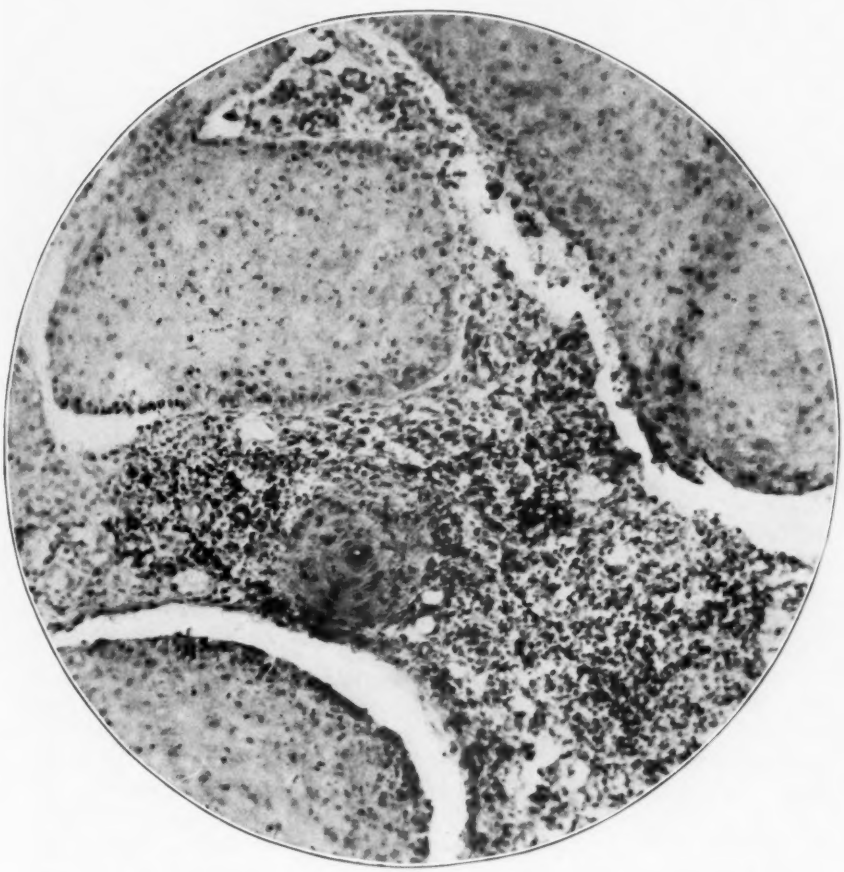

Fig. 3 (case 6).—Histologic section of skin showing pearl cell epithelioma.

report was as follows: "Tissue from the mandible showed marked inflammatory reaction in the fibrous connective tissue and muscle, with thickening and proliferation of the surface mucosa extending downward into the inflammatory tissue." After removal of the root the lesion healed. There was some scarring of the cheek. The patient has now been well for one year.

CASE 7.—Mrs. E. H., aged 66, was referred to us with a diagnosis of "basal cell carcinoma of the chin." For the previous five months she had had a crusted nodular ulcerating lesion on the skin on the right mental region, from which pus exuded from time to time. Examination revealed a granular lesion about 1.5 cm. in diameter, with considerable induration, together with a carious nonvital lower right lateral incisor tooth. Roentgenograms showed a large rarefied area around this incisor. As there were seven other lower anterior teeth present which were in

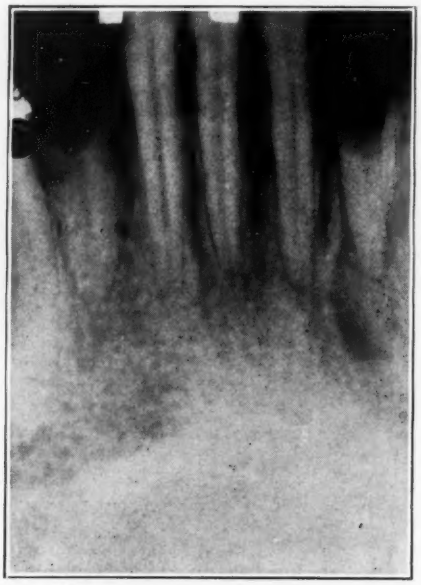

Fig. 4 (case 7).—Roentgenogram showing a rarefied area at the apex of the carious nonvital mandibular right lateral incisor. The cutaneous lesion was in the right mental region.

poor condition, all of the lower anterior teeth were extracted. The lesion healed after the extraction and has remained healed for eight months.

CASE 8.—C. D., a girl aged 20, was referred to us by a physician who stated that the patient was suffering from a "sore on the face." He had been treating it for the past five months. He also stated that he "thought perhaps it was a cyst." The patient presented an ulcerated, indurated granular lesion about 1 cm. in diameter in the skin over the angle of the right jaw. Dental examination revealed the lower right third molar tooth to be carious and nonvital. Roentgenograms showed a rarefied area around the apexes of this tooth. The histopathologic diagnosis from a section of the cutaneous lesion was "abscess." The tooth was extracted, and the lesion healed. The patient has remained well for one and a half years.

CASE 9.—Mrs. A. W., aged 47, according to the referring physician, for the past year had a lesion near the left ala of the nose from which pus exuded from time to

time. Examination revealed a discharging fistula a little to the left of the ala. The teeth were in poor condition, and many retained carious roots were present. Roentgenograms showed areas of rarefaction around most of the carious roots and teeth in the upper jaw. Around the root of the upper left cuspid was a large rarefied area, and a metallic probe, which was inserted in the fistula at the time of

Fig. 5 (case 9).—Roentgenogram showing a probe extending into the rarefied area at the apex of the tooth.

Fig. 6 (case 10).—Roentgenogram showing a diffuse rarefied area around the mandibular third molar.

taking the film, extended into the area around the apex of the cuspid tooth (fig. 5). This confirmed the clinical diagnosis of fistula from the pathologic area in the region of the cuspid. The teeth were extracted, and the lesion healed. The patient has remained well for fourteen months.

CASE 10.—H. C., a woman aged 23, had a small progressive lump appear in the skin adjacent to the region of the third molar tooth of the right mandible one and a half years previous to her admission to the hospital. There was no pain or discharge. It had been removed three months previous to admission but had not healed and had been draining ever since with a yellowish discharge. There was slight soreness. On admission it was observed that the patient had a fistulous opening with discharge in the lower right submaxillary molar region. The third molar was loose. Roentgenograms of this region showed loss of alveolar structure together with a diffuse rarefied area around the third molar (fig. 6); the rarefied area extended down about 1 cm. from the apexes. The tooth was extracted, and the alveolus curetted. The lesion healed uneventfully and has now been healed for five years.

CASE 11.—D. T. had a depressed lesion, the center of which was somewhat papular, in the skin over the left mandible. There was no apparent discharge. Examination of the mouth revealed a carious, nonvital molar tooth adjacent to the cutaneous lesion. Fibrosis and induration were present in the soft tissues of

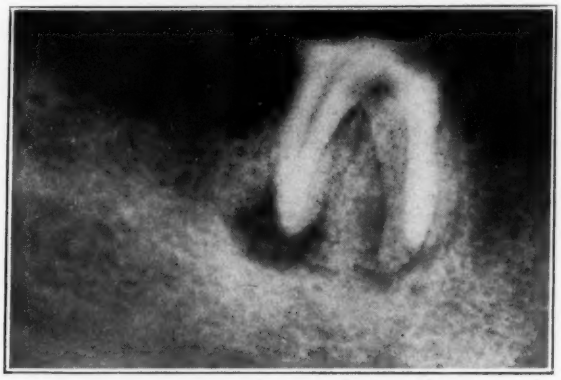

Fig. 7 (case 11).—Roentgenogram showing a rarefied area at the apex of the tooth adjacent to the cutaneous region.

the cheek between the alveolar process and the skin. Intraoral roentgenograms showed a rarefied area at the apex of the molar (fig. 7). A biopsy revealed "subcutaneous abscess." The tooth was extracted and the bone curetted. Uneventful healing and elimination of the cutaneous lesion followed.

CONCLUSIONS

1. A cutaneous fistula of dental origin may be mistaken for an epidermoid carcinoma.

2. The precursor of this facial cutaneous lesion is the dental alveolar abscess.

3. Intraoral and extraoral roentgenograms are valuable diagnostic adjuncts.

4. Treatment of such a lesion should consist of extraction of the offending tooth and curettement of the alveolus and contiguous infected granulation tissue and abscess.

PARAPSORIASIS: ITS RELATION TO MYCOSIS FUNGOIDES AND TUBERCULOSIS

A REVIEW OF FIFTY-TWO CASES

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It is the purpose of this paper to correlate, if possible, the clinical and histologic observations on various types of parapsoriasis and the relation of parapsoriasis to mycosis fungoides and other types of lymphoblastoma and to tuberculosis. Excellent articles presenting divergent views in regard to parapsoriasis and its relation to mycosis fungoides and containing reviews of the literature have recently been written by Keil [1] and McCarthy.[2] In addition, the clinical characteristics and classification of various types of parapsoriasis have been given by Civatte,[3] Fox and MacLeod,[4] MacLeod,[5] Ormsby [6] and Wise,[7] all of whom have been interested in this subject for decades. These writers all are agreed essentially in regard to classification, and Ormsby has stated the multiple synonyms that have been employed for the various types.

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3. Civatte, A.: Les parapsoriasis, in Darier, J.; Sabouraud, R.; Gougerot, H.; Milian, G.; Pautrier, L. M.; Ravaut, P.; Sézary, A., and Simon, C.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 7, pp. 686-723.

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5. MacLeod, J. M. H.: Parapsoriasis, Brit. J. Dermat. **44**:569-580 (Dec.) 1932.

6. Ormsby, O. S.: A Practical Treatise on Diseases of the Skin for the Use of Students and Practitioners, ed. 5, Philadelphia, Lea & Febiger, 1937, pp. 281-288.

7. Wise, F.: Parapsoriasis: Suggestions for Simplifying Its Nomenclature and Classifying Its Clinical Varieties for Teaching Purposes, New York State J. Med. **28**:901-908 (Aug. 1) 1928.

We shall divide parapsoriasis into parapsoriasis guttata, parapsoriasis en plaques and parakeratosis variegata. Most authors group pityriasis lichenoides et varioliformis acuta (Habermann) as a subvariety of parapsoriasis guttata.[8] Parapsoriasis atrophicans of Kreibich can probably be regarded as a variety of the guttate type. In this paper we shall not attempt to repeat in detail clinical descriptions of the various types of parapsoriasis as given by the authors mentioned in the preceding paragraph.

MATERIAL STUDIED

This study is based on 52 cases of parapsoriasis encountered at the Mayo Clinic in which histologic studies were made. Diagnosis was confirmed in most cases by other members of the Section on Dermatology after presentation at conference. In many of the cases diagnosis of parapsoriasis had been made elsewhere, and several of the cases had been presented at dermatologic meetings. In addition to the 52 cases of various types of parapsoriasis there were several cases in which a tentative clinical diagnosis of one form of parapsoriasis was made but in which the condition proved, especially in the light of histologic studies, to be one of several other dermatoses. There were 3 cases of what was regarded as parapsoriasis en plaques in which the histopathologic picture was definitely that of mycosis fungoides and 3 other cases in which clinical findings favored early mycosis fungoides rather than parapsoriasis en plaques and the findings were substantiated by histologic studies. On the basis of a preliminary review of most of the 52 cases McCarthy has quoted the preliminary impressions of the senior author. These impressions, as a result of more intensive study of this whole question, have undergone amplification and modification, as will become evident later in this paper.

PARAPSORIASIS GUTTATA (PITYRIASIS LICHENOIDES CHRONICA)

In 24 of the 52 cases the disease was classified as parapsoriasis guttata. Fourteen of the patients were females and 10 were males. The average age of onset was 39 years, and the average duration of the disease at the time of examination was six years. One patient, a girl aged 7 years, had had the disease for one year. The oldest patient, a man aged 64, had had lesions for only a month. A woman aged 57 had had cutaneous lesions since the age of 22, or for thirty-five years. One patient complained of severe pruritus and 13 patients of mild pruritus.

8. Gross, P.: Pityriasis Lichenoides et Varioliformis Acuta (a Variety of Parapsoriasis), Arch. Dermat. & Syph. **23**:33-48 (Jan.) 1931. Ormsby.[6]

It was possible to follow 8 of the 24 patients. Involution of the disease occurred in 4 of them; in 1 instance the condition cleared up a year after the patient left the clinic, although occasionally over a period of ten years there had been recurrences of a few lesions. At the time this paper is written, a second patient has remained free of lesions for seven years

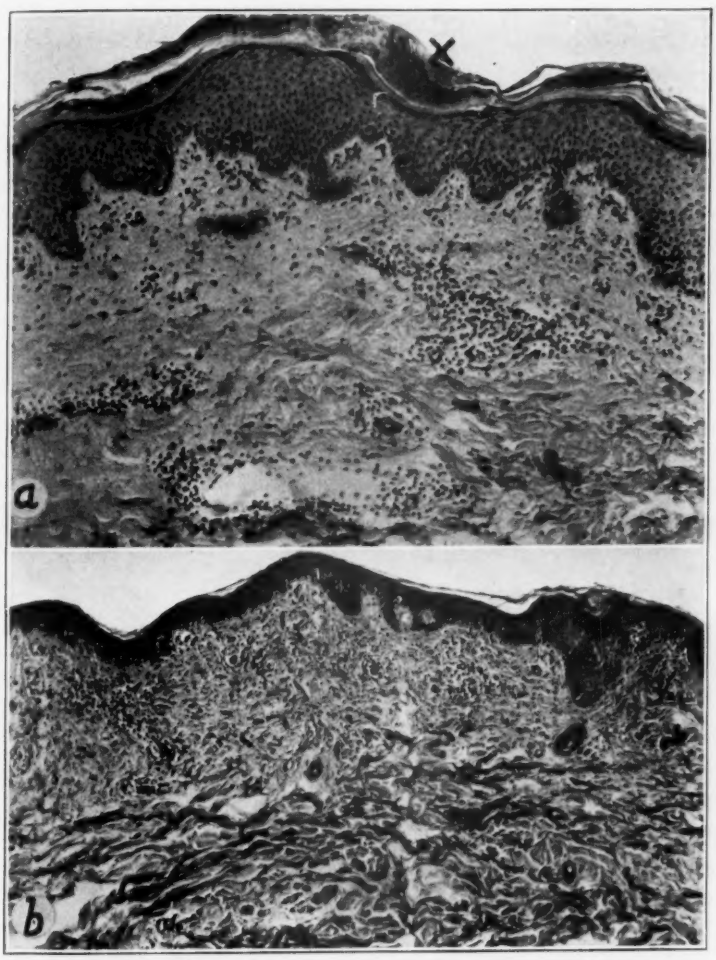

Fig. 1.—Parapsoriasis guttata: *a*, parakeratosis with beginning microabscess (*X*), moderate degree of acanthosis and perivascular infiltrate in the cutis (× 80); *b*, hyperkeratosis, slight parakeratosis, early liquefaction degeneration of basal cell layer in several areas and mild degree of perivascular infiltrate in the cutis (× 60).

and a third for six months, and a fourth has had remissions and recurrences over a period of eight years. Another patient at the time of examination gave a history of remissions of the disease during the sum-

mer subsequent to exposure to sunlight. Involution of the parapsoriasis occurred after roentgen therapy in 2 cases and after use of ammoniated mercury ointment or mercury inunctions in 2 other cases.

The histopathologic changes seen in any type of parapsoriasis are not diagnostic, but they are of value in distinguishing parapsoriasis from other dermatoses, including psoriasis and lichen planus, with which it sometimes is confused (fig. 1). The histopathologic changes observed in parapsoriasis guttata in the cases in this series were comparable to those described by McCarthy. There usually is parakeratosis, although occasionally this may be absent. Parakeratosis occurs in isolated foci rather than in a continuous layer, as is commonly seen in psoriasis. There are a slight to moderate degree of acanthosis and some elongation of the papillary bodies, but clubbing of the papillary bodies, as seen in psoriasis, is not present. Although edema in the epidermis is chiefly intracellular, intercellular edema and small areas of spongiosis sometimes are encountered. The early lesions tend to show more edema and cellular infiltrate and less atrophy than the older lesions. There may be slight edema of the papillary bodies, but diffuse edema of the upper portions of the cutis, which frequently is seen in the en plaques type, does not occur. Unlike the histopathologic picture of psoriasis, spotted areas of liquefaction degeneration of the basal cell layer are seen in association with infiltrate in the upper part of the cutis. The infiltrate is chiefly perivascular and is composed chiefly of lymphocytes and monocytes. In our series, contrary to Civatte's observation, polymorphonuclear leukocytes and eosinophils were present in every case. Migration of leukocytes through the epidermis occurs, resulting in microabscesses which, however, are smaller and not so prominent as those seen in psoriasis. The capillaries may be dilated but are without any apparent rigidity or tortuosity. In the later stages of parapsoriasis guttata mild atrophic changes occur in the epidermis. Elastic tissue as a rule is frayed and splintered but is not destroyed.

PARAPSORIASIS VARIOLIFORMIS: PITYRIASIS LICHENOIDES VARIOLIFORMIS ACUTA (HABERMANN)

In only 5 of the 52 cases of parapsoriasis was diagnosis made of parapsoriasis varioliformis. We have encountered this condition, however, among children, in several additional cases at the clinic in which for various reasons specimens for biopsy were not taken. The average age of onset in the 5 cases was 26 years. Pruritus was present in only 1 case. In 2 of the 5 cases the disease began as parapsoriasis varioliformis,

only later to assume features of parapsoriasis guttata. In 2 of the 5 there were remissions; a woman aged 27 was free from the disease in seven months, and a man aged 69, who had had recurrent attacks of parapsoriasis varioliformis for thirty-five years, returned to the clinic with complete remission after one year.

The diagnosis of parapsoriasis varioliformis is often difficult to make and often depends on exclusion of other dermatoses which the disease may simulate. If it were not for the association of parapsoriasis varioliformis and parapsoriasis guttata in the same case, we should be inclined to agree with the point of view of earlier writers on this subject that parapsoriasis varioliformis was not related to the group of parapsoriasis. The clinical and histologic changes in many respects are different.[9] In parapsoriasis varioliformis there usually is an acute onset characterized by multiplicity of lesions, including papular, papulosquamous, vesicular, bullous, hemorrhagic and even necrotic lesions. There may be associated fever or glandular enlargement. The clinical picture may simulate that of varicella, variola or malignant syphilis, but it lacks the toxemic manifestations of the first two conditions and the concomitant observations in regard to syphilis. Michelson, in discussing the paper of Senear and Oliver,[9] spoke of parapsoriasis varioliformis as a form of exanthem which had certain characteristics of a trichophytid. The following case illustrates the difficulties of diagnosis in this group.

Case 1.—A man aged 36 was examined at the clinic in August 1930 because of bullous lesions on the hands of nine months' duration. Hematoporphyrin was present in the urine, and diagnosis was made of epidermolysis bullosa. The patient returned to the clinic in February 1941 because of five years' history of recurrent attacks of vesiculation, pustulation and papules followed in three to five days by fever and chills lasting from three to ten days. After involution of the lesions pigmented spots persisted for two months and there were residual varioliform scars. The attacks occurred in the fall and early spring.

The patient apparently had trichophytosis with definite associated changes in the nails. The eruption was first interpreted as a trichophytid. The multiple character of the eruption is evident in figure 2. There were multiple small petechial necrotic lesions about the hairs as well as a generalized papulovesicular eruption. Fungi were never demonstrable in material from either the finger nails or the toe nails or from vesicles on the hands, and cultures were negative for fungi. There was no response to therapy for fungous infection. The patient was examined again in February 1942, at which time the lesions on the trunk appeared to be more of the guttate variety than previously, while those on the extremities remained varioliform. The patient had returned to the clinic because of the development of early signs of Buerger's disease. The histopathologic changes as

9. Senear, F. E., and Oliver, E. A.: Pityriasis Lichenoides et Varioliformis Acuta (Habermann), Arch. Dermat. & Syph. **23**:12-28 (Jan.) 1931.

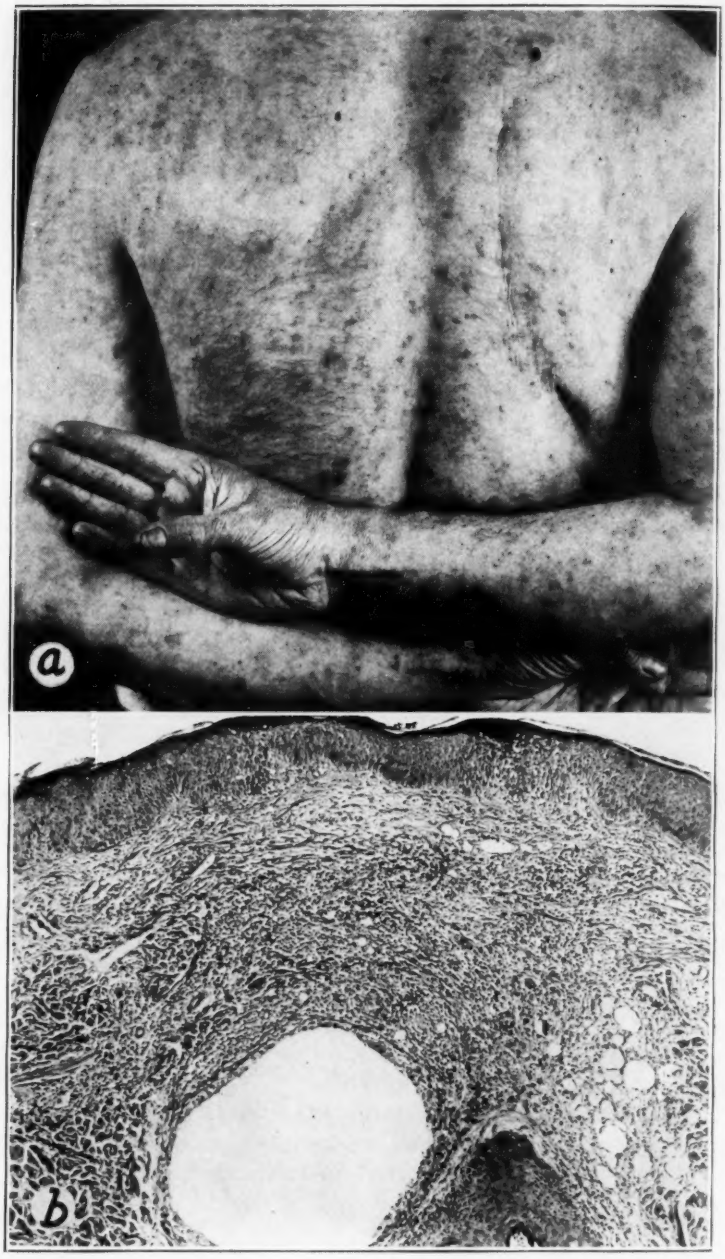

Fig. 2.—Parapsoriasis varioliformis. Note the multiple types of lesions. Histopathologic changes are: early formation of vesicles in the epidermis and dense infiltrate with foreign body giant cell reaction in relation to hair follicles and the cutis (× 55).

shown in figure 2 represented early formation of vesicles in the epidermis together with a foreign body giant cell reaction in relation to hair follicle and cyst in the cutis. There was no evidence of true tubercle formation.

In the early stages the histopathologic changes observed in parapsoriasis varioliformis are those of an acute inflammatory process involving the epidermis and the upper portions of the cutis. There is decided intracellular edema, resulting in formation of vesicles similar to those seen in varicella and variola together with hydropic degeneration of the rete cells. Migration of large numbers of polymorphonuclear leukocytes and lymphocytes throughout the epidermis results in the formation of abscesses. The infiltrate in the cutis may be so considerable as to effect destruction of the epidermis above it, and there is formation of a necrotic crust. The infiltrate is composed not only of lymphocytes and leukocytes but also of eosinophils, basophils and plasma cells. When follicular lesions are prominent, there is often a foreign body giant cell reaction which is to be distinguished from tubercle formation as seen in tuberculosis. The histopathologic changes in parapsoriasis varioliformis naturally vary according to the character of the lesions studied, whether vesicular or papular and whether acute or chronic. When the infiltrate is considerable, there is destruction of the elastic tissue. Almkvist found that the early papular lesions of parapsoriasis varioliformis correspond histologically to the changes present in parapsoriasis guttata; in 2 of our cases of parapsoriasis varioliformis in which the lesions had been present for many years and had assumed clinical features of the guttate variety, the histopathologic changes of the two conditions were indistinguishable.

PARAPSORIASIS EN PLAQUES

In 20 of the 52 cases in our series the disease was classified as parapsoriasis en plaques (fig. 3). In contrast to the incidence of the guttate type of parapsoriasis, 14 of the patients with this disease were males and 6 were females. The youngest patient was 22 years of age and the oldest 64; the average age was 39. The average duration of the disease at the time the patients were examined at the clinic was nine and five-tenths years. One patient aged 22 had had lesions for only five weeks. Another, a man aged 62, had had the disease for forty-eight years; the lesions had started on the thighs at the age of 14 and gradually had spread. Pruritus was severe in 1 case and of slight degree in 9 other cases. Many of the patients in this group were observed on more than one occasion, but it was possible to follow only 5 by correspondence over a period of four to twelve years. Five patients gave history of remission of the disease each spring or summer. In 1 patient the disease

cleared up entirely, and that patient at the time of this report has remained free from symptoms for two years. Exposure to the sun in the summer accounts for remissions in this season.

The histopathologic changes occurring in parapsoriasis en plaques are similar to those seen in parapsoriasis guttata (figs. 4 and 5). Gans [10] emphasized the wide band of edema which involves not only the papillary bodies but the upper portion of the cutis and which usually is demarcated sharply. McCarthy also observed that this feature predominates in

Fig. 3.—Parapsoriasis en plaques in a woman aged 52 who had extensive generalized eruption of many years' duration, with absence of itching, lack of induration in the lesions and no evidence of mycosis fungoides (fig. 5 *b* shows the histopathologic picture).

parapsoriasis en plaques. A review of the microscopic sections of tissue made in this series of cases revealed that edema of this type is present in practically all cases of parapsoriasis en plaques but that it does not as a rule stand out prominently, nor is it demarcated as sharply as described

10. Gans, O.: Histologie der Hautkrankheiten. Die Gewebsveränderungen in der kranken Haut unter Berückssichtigung ihrer Entstehung und ihres Ablaufs, Berlin, Julius Springer, 1925, vol. 1, pp. 309-316.

by Gans. In the plaque type parakeratosis may be present, but as a rule it is absent except when a considerable degree of infiltrate is present in the cutis. The epidermis in the center of the plaque often is thinned and displays atrophy of varying degrees. There is a moderate acanthosis at the edge of the plaque, as a rule without any papillomatosis or increase in the length of the rete ridges. Edema of the epidermis is not prominent

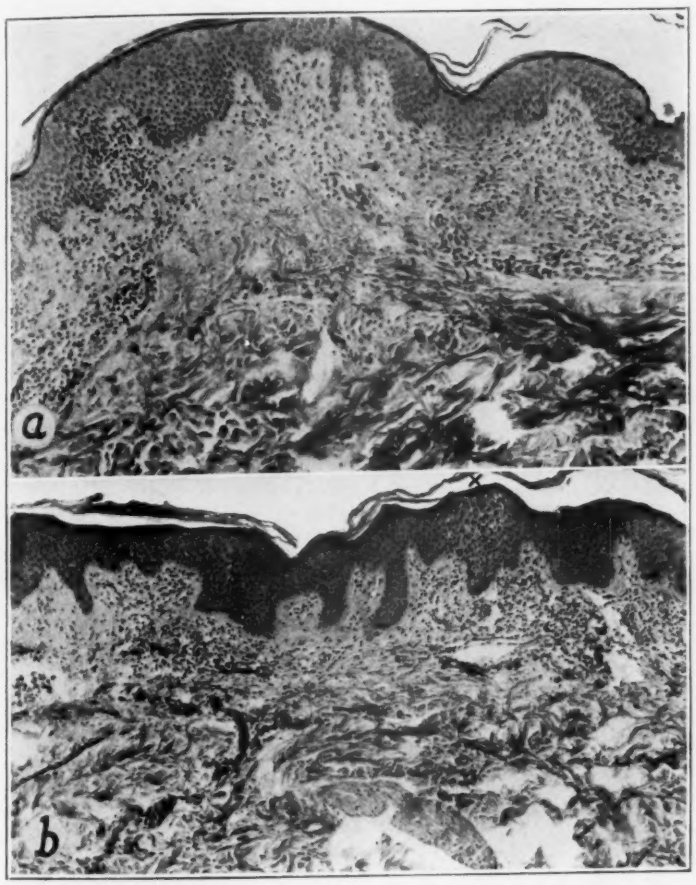

Fig. 4.—Parapsoriasis en plaques. In *a*, note the absence of parakeratosis, the slight degree of acanthosis, liquefaction degeneration of the basal cell layer at the left and the edema and sparse infiltrate in the upper part of the cutis (× 80); in *b* are shown alternate areas of parakeratosis and hyperkeratosis, with beginning spongiosis just below *X* (× 60).

but occurs in spotted areas and results in small regions of spongiosis. Occasionally small microabscesses are seen (fig. 5*b*) and a slight degree of liquefaction degeneration of the basal cell layer occurs. The edema in the cutis varies in direct proportion to the amount of cellular infiltrate. The infiltrate is chiefly perivascular and is limited chiefly to the upper

parts of the cutis. Lymphocytes predominate, although in all the cases of our series polymorphonuclear leukocytes were present; a few eosinophils, occasional basophils and plasma cells were found, as well as many mononuclear cells. Dilatation of the capillaries is not a prominent fea-

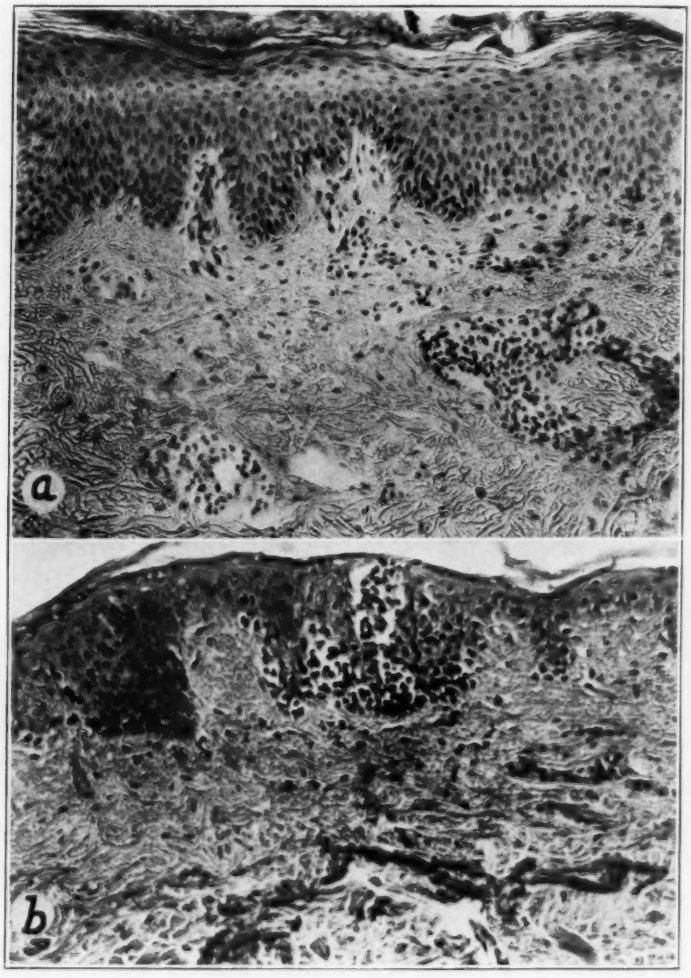

Fig. 5.—Parapsoriasis en plaques: *a*, parakeratosis, acanthosis with flattening of papillary bodies, edema in the upper part of the cutis (× 150); *b*, migration of lymphocytes through the epidermis forming early microabscess, edema and homogenization of connective tissue in the upper part of the cutis and relative absence of any infiltrate in the cutis (× 190).

ture; collagen and elastic fibers are separated by the edema but not destroyed. In our cases proliferative changes were not present in the vessel walls.

PARAKERATOSIS VARIEGATA (RETIFORM VARIETY OF PARAPSORIASIS, PARAPSORIASIS LICHENOIDES [BROCQ], LICHEN VARIEGATUS [CROCKER])

McCarthy would abandon this form of parapsoriasis believing that the manifestations in some cases have been atypical forms of lichen planus or parapsoriasis guttata and that in other cases the disease has been lymphoblastoma. Although Civatte separated parapsoriasis lichenoides and lichen variegatus from parapsoriasis variegata, most authors regard the lichenoid or retiform type as representing merely one phase of parakeratosis variegata, and with the latter view we are in accord. We believe that parakeratosis variegata is a distinct but relatively rare type of parapsoriasis. Of the 52 cases in our series, there were 3 in which we felt the condition belonged in this group.

CASE 2.—The patient was a child 5 years of age who for three years had had a generalized eruption with much pigmentation. The retiform arrangement of the lesions together with the histopathologic changes was consistent with the diagnosis of parakeratosis variegata, and it was possible to rule out urticaria pigmentosa, angioma serpiginosum and various purpuric dermatoses which were considered in differential diagnosis.

CASE 3.—The patient, a physician aged 59, was first seen at the clinic in July 1930, at which time diagnosis of parakeratosis variegata was made by Dr. W. H. Goeckerman; this diagnosis was confirmed by Dr. P. A. O'Leary in 1933. The results of histologic studies made in 1930 were consistent with this diagnosis. The patient showed slight improvement after pilocarpine sweats. From replies to letters of inquiry it was learned that he had been examined by Dr. O. S. Ormsby also in 1930 [11] and that the condition was regarded as a classic example of parakeratosis variegata. The patient was seen again at the clinic in September 1942. He still had parapsoriasis, which had become more marked, and presented multiform types of lesions. A specimen for biopsy unfortunately was taken from an excoriated lesion and proved unsatisfactory for distinguishing between parapsoriasis and early mycosis fungoides. The patient had an amputation of the right hand because of recurrent squamous cell epitheliomas, grade 2 to 3. He also had arsenical keratoses on the palms and soles, although he gave no history of ingestion of arsenic. The parapsoriasis in this case started when the patient was 27 years of age, and he has now been observed for forty-two years without definite evidence of lymphoblastomatous change.

CASE 4.—In this case the diagnosis is not so clearcut as in cases 2 and 3. A woman aged 49 first was seen at the clinic in 1934 because of mild diabetes. A year previously she had bruised her ankle and ecchymosis had developed. Four weeks before coming to the clinic she took insulin and noticed urticaria wheals at the site of each injection. The patient presented a papular, pigmented, lichenified, retiform and somewhat purpuric-like eruption occurring chiefly on the upper part of the thighs but extending down the legs. There were a few lesions on the trunk and arms (fig. 6); the latter had developed only after the patient had started taking the injections of insulin. The histopathologic picture was consistent with that of parakeratosis variegata. The presence of hemosiderin could

11. Ormsby,[6] fig. 108, p. 282.

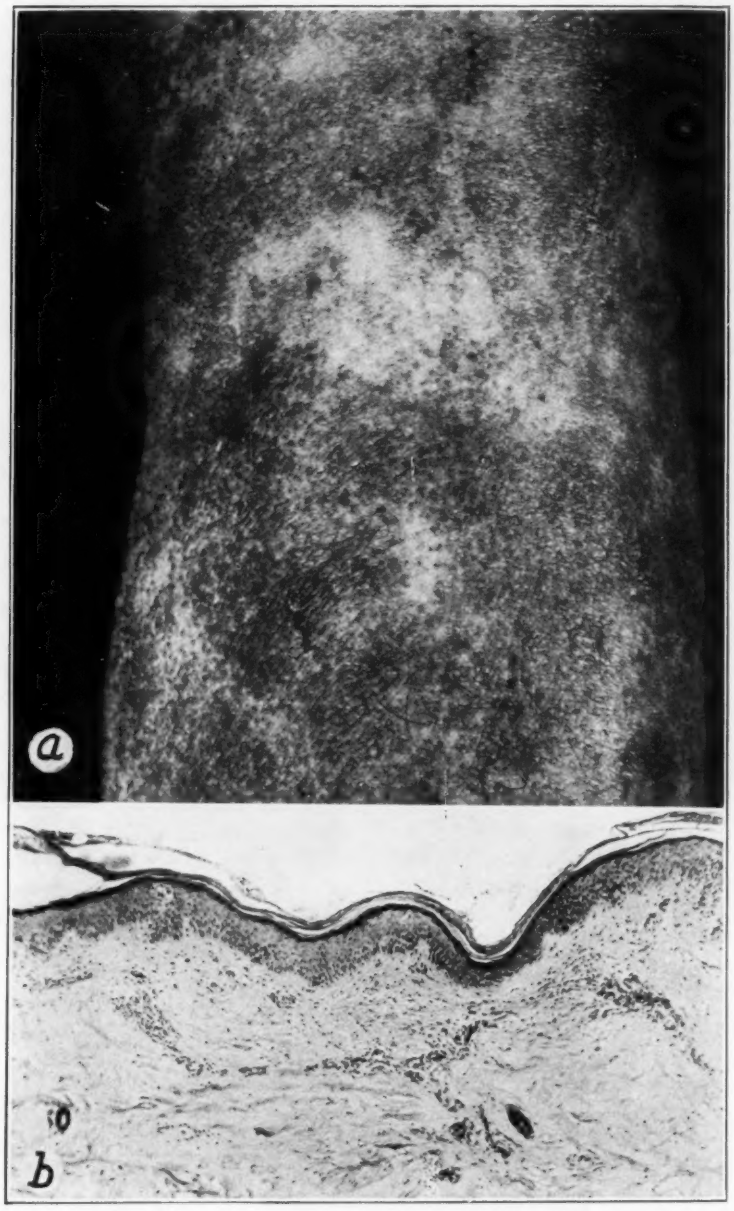

Fig. 6.—Parakeratosis variegata (retiform or lichenoid type from the leg). In *a*, note the lichenoid papules, areas with atrophy, pigmentation, netlike arrangement and changes simulating poikiloderma, in *b* are shown histopathologic changes similar to those of parapsoriasis guttata but including in addition dilatation of the capillaries.

not be demonstrated, which ruled out Schamberg's disease and purpuric pigmentary lichenoid dermatitis of Gougerot and Blum. The patient received mercury inunctions, and when she returned in July 1937 she stated that the cutaneous lesions had cleared up in a month. Her general examinations in 1932, 1934 and 1937 failed to reveal evidence of lymphoblastoma but disclosed on each occasion mild diabetes and at one time mild arthritis in the shoulder. It is possible that the patient had a drug eruption from insulin, but the histopathologic changes were not those usually seen in dermatitis medicamentosa and were consistent with those in parakeratosis variegata.

The histopathologic changes in parakeratosis variegata resemble those seen in parapsoriasis guttata with the exceptions that there is decided dilatation of the capillaries and that liquefaction degeneration of the basal cell layer is more prominent. The infiltrate in the cutis may form an almost continuous layer just beneath the epidermis. The character of the infiltrate is the same as that in the other types of parapsoriasis. There may be definite atrophy of the epidermis and some destruction of the elastic tissue. Only in case 2 was there any evidence of deposition of hemosiderin. In this disease the histopathologic changes differ from those in poikiloderma only in the milder degree of inflammatory reaction and the relative absence of atrophy and also in the presence of parakeratosis, which is not common in poikiloderma. In none of the cases was there any histologic evidence of lymphoblastoma.

MacLeod stated that poikiloderma of Jacobi can be distinguished from parapsoriasis because it has two distinct stages, one inflammatory and the other atrophic. Nekam [12] emphasized the difficulty in distinguishing between the two diseases. Acrodermatitis chronica atrophicans can be distinguished from parakeratosis variegata by the different histopathologic changes which are diagnostic for acrodermatitis chronica atrophicans. We concur, however, with McCarthy that in many cases parakeratosis variegata is diagnosed erroneously. An example which may be cited was a case presented by Omens and Omens [13] in which histologic studies revealed a characteristic picture of the atrophic stage of lichen planus and in which further scrutiny revealed clinical lesions of lichen planus.

TRANSITIONAL FORMS

MacLeod [5] mentioned that cases occur in which guttate lesions are associated with lesions of an en plaques type and also that a retiform or reticulated eruption has been associated with lesions of an en plaques

12. Nekam, L., Jr.: A propos des difficultés de diagnostic entre le parapsoriasis lichenoïde et le poikilodermie, Ann. de dermat. et syph. **9**:31-49 (Jan.) 1938.

13. Omens, D. V., and Omens, H. D.: A Case for Diagnosis (Parapsoriasis?), Arch. Dermat. & Syph. **44**:300-301 (Aug.) 1941.

type. Muschter [13a] described a case in which all three types of parapsoriasis occurred and referred to numerous cases reported in earlier medical literature. It is of interest, therefore, that in the large series of cases studied by McCarthy the manifestations of disease have remained true to type and that there has been no combination of lesions of guttate and en plaques types. This has been our experience also with the series of 52 cases which we are reporting. We have mentioned previously in this paper the reasons for regarding parapsoriasis varioliformis as a form of parapsoriasis guttata.

DIAGNOSIS

Distinction of various types of parapsoriasis from psoriasis, lichen planus and acrodermatitis chronica atrophicans can be made on the basis of the distinctive histopathologic picture in the last-mentioned conditions. Reference to the differential diagnosis has already been made in the description of the individual types of parapsoriasis. Parakeratosis variegata may be difficult to distinguish from the poikiloderma of Jacobi. It is questionable, however, whether the latter condition is a distinct entity, because in recent years the picture of poikiloderma has been described in association with a great many dermatoses, including lymphoblastoma, parapsoriasis, lupus erythematosus and dermatomyositis, and syphilis.

RELATION OF PARAPSORIASIS TO MYCOSIS FUNGOIDES AND THEIR DIFFERENTIATION

Keil recently stated after a review of the literature that in practically all cases parapsoriasis en plaques represents an incipient stage of mycosis fungoides, whereas McCarthy, on the basis of a histologic study in a large series of cases, expressed the belief that parapsoriasis guttata and parapsoriasis en plaques remain as such and eventuate in neither mycosis fungoides nor any other lymphoblastoma. Keil and McCarthy were in agreement regarding the close relation of so-called parakeratosis variegata to poikiloderma and mycosis fungoides. There is almost uniform agreement among physicians that parapsoriasis guttata does not eventuate in mycosis fungoides or lymphoblastoma. McCarthy would emphasize that when diagnosis of parapsoriasis is made clinically and the disease proves histologically to be mycosis fungoides in an early stage there has been a mistake in clinical diagnosis and that the percentage of cases of parapsoriasis en plaques in which the disease changes to mycosis fungoides is extremely small. A case presented by Cornbleet and Schorr,[14] which one of us (H. M.) discussed, is an example of this.

13a. Muschter: Ueber einen Fall von Parapsoriasis (sämtliche drei Typen in einem Fall vereint), Arch. f. Dermat. u. Syph. **121**:918-924, 1916.

14. Cornbleet, T., and Schorr, H. C.: Case for Diagnosis—Lymphoblastoma? Parapsoriasis? Arch. Dermat. & Syph., to be published.

In many of the cases in the literature that were cited by Keil as illustrating transition from parapsoriasis to mycosis fungoides the diagnosis was based in the beginning on clinical findings only. On the other hand, there are some cases in which the disease apparently starts as parapsoriasis en plaques and eventuates in mycosis fungoides. Gougerot and Burnier [15] described such a case, in which the lesions were of eighteen years' duration and in which there was no itching. The histopathologic observations as studied by Eliascheff were consistent with the diagnosis of parapsoriasis en plaques, and there was no evidence of mycosis fungoides. Four years later there were poikiloderma-like changes in the skin, and only six years after the first biopsy histologic changes of mycosis fungoides appeared and the clinical appearance then became that of mycosis fungoides.

One of us (H. M.)[16] formerly thought that parapsoriasis en plaques and parakeratosis variegata frequently were prodromal manifestations of one of the lymphoblastomas, particularly mycosis fungoides. When, however, we analyzed the data in our series of 52 cases of parapsoriasis, in no case was there evidence of change to any of the lymphoblastomas. Approximately a third of the 52 patients have been followed for one to twelve years. The duration of the disease has been as long as forty-eight years without any history of lymphoblastomatous change. It must be remembered that there were, in addition, 6 cases in 3 of which the disease was regarded clinically as parapsoriasis en plaques and in 3 as an early premycotic stage of mycosis fungoides; in all 6 there were evident the histopathologic changes of mycosis fungoides. However, if the 3 cases of mycosis fungoides were added to the parapsoriasis group, it could scarcely be said that parapsoriasis was a frequent prodromal manifestation of mycosis fungoides. In an approach to the question from the opposite direction, among more than 150 specimens taken for biopsy from which a diagnosis of mycosis fungoides was made there were only 6 for which a diagnosis of parapsoriasis en plaques or parakeratosis variegata was considered seriously.

McCarthy gave detailed minute criteria for clinical distinction between parapsoriasis en plaques and the early stages of mycosis fungoides. He justly emphasized that in parapsoriasis en plaques there is lack of indura-

15. Gougerot, H., and Burnier: Parapsoriasis en plaques avec poïkilodermie; transformation ultérieure en mycosis fungoïde, Bull. Soc. franç. de dermat. et syph. **41**:1528-1535 (July) 1934.

16. Montgomery, H.: Mycosis Fungoides, Lymphoblastoma of the Skin, and Allied Conditions as General Diseases, in Christian, H. A., and MacKenzie, J.: Oxford Medicine, New York, Oxford University Press, 1920, vol. 4, pt. 1, pp. 44 (1)-44 (19).

tion and that the plaques tend to fade out into the normal skin rather than to have sharply defined margins, as usually seen in mycosis fungoides. In the early stages of mycosis fungoides, however, many lesions are eczematoid and even transitory. In our series it was striking that more than half of the patients who had parapsoriasis of various types complained of pruritus, usually, it is true, of only a slight degree. The great majority had a definite itching rather than a mere feeling of discomfort, which McCarthy described as a common cause of complaint in parapsoriasis. Although pruritus is usually an early and a prominent symptom in mycosis fungoides, we have encountered many cases in which there was no pruritus over a period of a great many years. The duration of the disease is of relatively little value in distinguishing between the two conditions because mycosis fungoides may remain in the early premycotic stage for many years without giving evidence of tumor formation, ulceration or any appreciable progression. It should be admitted, therefore, that in some cases clinical distinction between premycotic mycosis fungoides and parapsoriasis en plaques becomes difficult if not impossible.

The histopathologic diagnosis of mycosis fungoides in its early stages is based on demonstration of an infiltrate composed of a multiplicity of cell types, with pyknosis and karyorrhexis of the individual cells and clumping of the cells. A somewhat similar picture with clumping of endothelial cells is seen in atopic eczema or generalized neurodermatitis; the two conditions may be difficult to distinguish. The difficulty is especially great when eczematoid changes or early eczematoid plaques in the early stages of mycosis fungoides are present, because these plaques often fail to present the histopathologic picture of the disease and often prove to be transitory, disappearing spontaneously.

It is possible to explain the difficulty in clinical and histologic distinction between parapsoriasis and the early stages of mycosis fungoides. The histopathologic changes in mycosis fungoides in the beginning are inflammatory. The same is true in Kaposi's sarcoma. It is only in the later stages that transition toward lymphoblastoma and fibrosarcoma respectively becomes apparent. One of us (H. M.) has emphasized previously that any chronic dermatosis or benign inflammatory process which develops as the result of chronic irritation may eventuate after a period of months or years in malignant lymphoblastoma or, as Fischer-Wasels has shown, that a benign or infectious process through chronic irritation may eventuate in epithelioma. Chronic ulcers of the leg are examples of this change. The percentage incidence of cases in which the phenomenon occurs, however, is very small, and none of these conditions of disease should be grouped with precancerous dermatoses.

RELATION OF PARAPSORIASIS TO TUBERCULOSIS

Civatte [17] formerly expressed the opinion that parapsoriasis as a whole might be of tuberculous causation, but in his more recent article [3] he questioned whether there is any tuberculous causative factor. Pick,[18] in 1904, described an unusually extensive generalized exanthematous lichenoid tuberculid. Civatte described 3 cases of tuberculids resembling parapsoriasis, and Milian and Pinard [19] reported a case of generalized eruption which they felt belonged with Civatte's cases but in which, in addition, there were telangiectatic and purpuric lesions. One of us (H. M.) has studied several cases which, in retrospect, belong with this group; some of these cases have been reported as instances of lupus miliaris disseminatus; [20] in none of them were there lesions on the face. Lesions of this type, which have been described as lichenoid tuberculids,[21] clinically may resemble parakeratosis variegata or the en plaques type of parapsoriasis with poikiloderma-like changes. They are, however, true forms of hematogenous tuberculosis and have nothing to do with parapsoriasis.

SUMMARY AND CONCLUSIONS

Parapsoriasis guttata persists as such over a period of many years, although occasional remissions may occur. In a few instances cure has resulted either spontaneously or subsequent to use of various therapeutic measures, and this is true of parapsoriasis en plaques also. Parapsoriasis varioliformis is a subvariety of parapsoriasis guttata; in a considerable number of cases there is spontaneous involution within a few weeks or months, and in others the disease persists with remissions and exacerbations or changes to parapsoriasis guttata. Parakeratosis variegata is a definite but rare type of parapsoriasis. Parapsoriasis en plaques and parakeratosis variegata rarely eventuate in mycosis fungoides or other forms of lymphoblastoma. They should not be regarded as prelymphoblastomatous diseases. Clinical distinction between parapsoriasis en plaques or parakeratosis variegata and the early phases of lympho-

17. Civatte, A.: Note pour servir à l'étude des tuberculides papulosquameuses. Trois cas de tuberculides à forme de parapsoriasis, Ann. de dermat. et syph. **37**:209-230, 1906.

18. Pick, W.: Ueber ein eigenartiges lichenoides Exanthem, Arch. f. Dermat. u. Syph. **69**:411-424, 1904.

19. Milian and Pinard: Parapsoriasis en gouttes, sa nature tuberculeuse, Ann. de dermat. et syph. **38**:477, 1907.

20. Montgomery, H.: Unusual Cutaneous Tuberculosis (Hematogenous in Type) Proved by Demonstration of Bacilli of Tuberculosis in the Skin, M. Clin. North America **19**:611-618 (Sept.) 1935.

21. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 6, Philadelphia, Lea & Febiger, 1942, to be published.

blastoma, especially the earlier stages of mycosis fungoides, may be impossible. Histopathologic studies frequently reveal that a disease diagnosed as parapsoriasis actually is one of the lymphoblastomas. Parapsoriasis guttata does not eventuate in mycosis fungoides. Although the histopathologic changes in the various types of parapsoriasis are not diagnostic, histologic studies are of value in distinguishing parapsoriasis from psoriasis, lichen planus and acrodermatitis chronica atrophicans, all of which have distinctive histopathologic features. There have been cases in which generalized lichenoid tuberculid (lupus miliaris disseminatus) in the past has been confused with parapsoriasis, but these types can be distinguished on histologic examination. There is no evidence of a tuberculous causation for parapsoriasis. The cause of parapsoriasis remains unknown.

PATHOGENESIS OF SYNOVIAL LESIONS OF THE SKIN

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Synovial lesions of the skin are of interest because of their rarity and because of the existing controversy as to their origin. They are usually located on the fingers and toes, in the vicinity of a joint, and are characterized by cystlike tumors that produce a globular elevation of the skin and contain a clear, colorless, viscid fluid.

Hyde,[1] in 1883, was the first to give a comprehensive description of these lesions. In 1888, in the second edition of his book,[2] he mentioned that Jones and Markins of St. Thomas Hospital, had presented several cases of this disease before the London Pathological Society. Hyde stated: "In every case the contents of the lesions are supplied by a synovial bursa beneath the skin, with which the lesion is either directly connected or in communication by a short sinus."

In 1913 Lingenfelter[3] reported a case in which he was unable to find any opening communicating with an articular space or other structure, nor could Ormsby[4] trace any such communication in his 4 cases, reported in the same year. Ormsby therefore considered the cause of the lesions an open question and strongly suggested an arthritic diathesis. Two cases were reported by Sutton[5] in 1916.

Jensen[6] offered the concept that these lesions have "their origin in embryonic arrests in the process of the development of periarticular tissue and synovial membranes." Jensen, however, regarded ganglial,

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

1. Hyde, J. N.: A Practical Treatise on Diseases of the Skin, for the Use of Students and Practitioners, Philadelphia, H. C. Lea's Son & Company, 1883, p. 423.

2. Hyde, J. N.: A Practical Treatise on Diseases of the Skin, for the Use of Students and Practitioners, ed. 2, Philadelphia, Lea Brothers & Co., 1888, p. 496.

3. Lingenfelter, G. P.: A Case for Diagnosis, J. Cutan. Dis. **31**:647, 1913.

4. Ormsby, O. S.: Synovial Lesions of the Skin, J. Cutan. Dis. **31**:943, 1913.

5. Sutton, R. L.: Radium in Treatment of Synovial Lesions of the Skin, J. A. M. A. **66**:565 (Feb. 19) 1916.

6. Jensen, D. R.: Ganglia and Synovial Cysts: Their Pathogenesis and Treatment, Ann. Surg. **105**:592 (April) 1937.

bursal and synovial lesions as identical in origin. In only 1 of his cases was there a synovial lesion of the skin.

In 1937 Gross [7] published a comprehensive survey of the 14 cases reported in the literature up to that time and added 8 more observed by himself. He stated the belief that the lesions were the result of a degenerative process, the product of a peculiar mucoid change in the connective tissue of the corium, leading to liquefaction and cyst formation, and considered local injuries and thrombosis of small arterial channels as likely causes of this local degeneration. He suggested, therefore, that synovial lesions of the skin should be termed "myxomatous-cutaneous cysts" and stated: "The idea that the cyst is an outpocketing of one of the serous membranes of a digit is wholly untenable." It is interesting to note, however, that in his article a photomicrograph (fig. 16) of a complete cyst is shown, at the deepest portion of which an indentation is visible, suggesting an entry to a tract.

The study of the pathogenesis of synovial lesions of the skin has been approached in various ways. The anatomic method did not produce an adequate explanation. A fibrous attachment to the joint has been shown to be present in 2 instances,[8] but failure to demonstrate any communication has been experienced by other investigators.[9] Some authors have pointed out that an artificial communication may result from sharp dissection, but only confusion has resulted from this approach to the problem.

Histologic examination of excised lesions has not led to conclusive results. MacKee and Andrews,[8a] Jensen [6] and Gross [7] described the lining of the cyst as fibrous. MacKee and Andrews observed occasional cells and nuclei on the inner surface of the cyst wall which they regarded as endothelial cells. Jensen said that the lesions were lined with a "waxy elastic tissue" and found no epithelial or endothelial cells. On the other hand, Weber and Freudenthal [10] observed a lining of from one to three rows of endothelial cells in several areas of the cavity.

Physicians who have had the experience of treating this condition have noted the rapidity with which recurrence follows surgical or electrosurgical methods of approach. The gelatinous material reappears after a short time and drains through the unhealed wound. Gross,[7]

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7. Gross, R. E.: Recurring Myxomatous, Cutaneous Cysts of the Fingers and Toes, Surg., Gynec. & Obst. **65**:289, 1937.

8. (*a*) MacKee, G. M., and Andrews, G. C.: Pathologic Histology of Synovial Lesions of the Skin, Arch. Dermat. & Syph. **5**:561 (May) 1922. (*b*) Jensen.[6]

9. (*a*) Montgomery, D. W., and Culver, G. D.: Pathologic Anatomy of Synovial Lesions of the Skin, Arch. Dermat. & Syph. **5**:329 (March) 1922. (*b*) Lingenfelter.[3] Ormsby.[4] Gross.[7]

10. Weber, E. P., and Freudenthal, W.: A Case of So-Called "Synovial Lesions," Proc. Roy. Soc. Med. **31**:345 (Feb.) 1938.

in offering his concept of myxomatous degeneration, admitted it is difficult to comprehend the continuation of this process after repeated excision or electrosurgical destruction.

MacKee and Andrews [11] were the first to examine such lesions roentgenographically. They found that soft tissue roentgenograms showed plainly a connection of the lesion with the joint cavity. In 1922 they reported a case in which a synovial cyst had been excised in its entirety. A fibrous cord was demonstrated firmly connecting the cyst capsule to the capsule of the joint. The connecting cord was hollow and tubular, but there was no definite continuous lumen leading from the cyst cavity to the cavity of the articulation.[8] Montgomery and Culver [9a] took exception to this concept. They maintained that the cystic lesions were the result of a colloid degeneration of a wart that had nothing to do with either the joints or the tendon sheaths. This interpretation evoked contradiction by MacKee and Andrews.[8a]

Savatard [12] reported 3 cases of periarticular fibroma of the skin ("synovial" lesions of the skin) and maintained that such lesions represent a cystic degeneration of a fibroma. In all 3 cases roentgenographic examination failed to reveal any connection between the lesions and the underlying structures.

Roentgenographic study of synovial lesions of the skin has produced conflicting results. Since the tumor is located in soft tissue, this approach alone is of very little help. We have felt, therefore, that a better understanding of the problem could be obtained from a roentgenogram taken immediately after the injection of a contrast fluid into the lesion. A search of the literature does not reveal any observation made with this method. Jensen [6] stated that in 1 of his cases iodized poppyseed oil was injected for roentgenologic study, but he failed to report the results obtained.

In the case described here roentgenographic studies were made of a synovial lesion of the skin after the injection of a contrast medium directly into the lesion.

REPORT OF A CASE

S. S., a Russian woman 42 years of age, came to the New York Skin and Cancer Unit in March 1941 presenting a tumefaction on the ulnar aspect of the left fifth finger of four months' duration. The lesion had appeared suddenly and had caused no pain or discomfort. It had reached its maximum of development in one month.

Examination revealed a globular swelling measuring 8 mm. in diameter on the ulnar aspect of the left fifth finger midway between the distal end of the

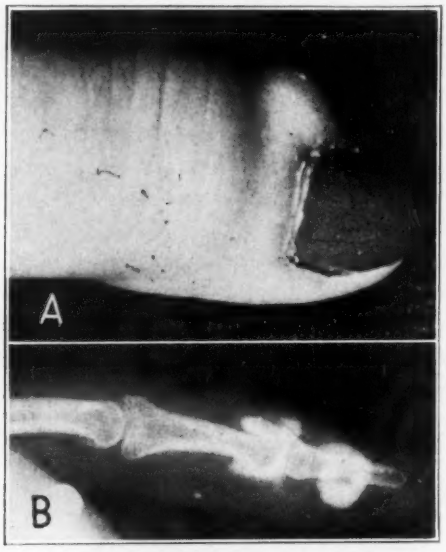
11. MacKee, G. M., and Andrews, G. C.: Synovial Lesions of the Skin, Arch. Dermat. & Syph. **4**:162 (Aug.) 1921.

12. Savatard, L.: Peri-Articular Fibroma of the Skin ("Synovial" Lesions of the Skin), Arch. Dermat. & Syph. **9**:441 (April) 1924.

finger and the distal interphalangeal joint. The lesion had a shiny, glassy appearance and transmitted light. It felt firm to the touch and could not be compressed by external pressure.

A roentgenogram taken on April 1 in the roentgenologic department of the New York Post-Graduate Medical School and Hospital showed a small soft tissue tumefaction the size of a pea on the left fifth finger.

On April 7 the contents of the lesion were aspirated with a large bore needle, and through the same opening diodrast sterile solution (Winthrop)—3,5-diiodo-4-pyridone-N-acetic acid and diethanolamine (35 per cent, weight/volume)—was injected with mild pressure so that it entirely replaced the aspirated fluid, which was clear, colorless, viscid and gelatinous in appearance. A roentgenogram taken immediately after the injection showed the contrast medium in the same cystlike nodule previously noted on the ulnar side close to the terminal interphalangeal joint and also in the joint itself.



A, a synovial lesion. *B*, a roentgenogram of the lesion taken after injection of a contrast medium.

The patient experienced transient pain from this procedure, which disappeared immediately after the contrast fluid had been expressed. She was seen two days later and the lesion was found to be refilled completely.

SUMMARY

The concept is offered that synovial lesions of the skin are due to an escape of synovial fluid from the joint cavity. One can only conjecture as to the cause and character of this opening into the articular space.

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COLLOID DEGENERATION (COLLAGEN DEGENERATION) OF THE SKIN

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Colloid degeneration of the skin, also known as colloid milium or hyaloma, is a rare dermatosis of unknown cause. It is characterized by discrete or confluent yellowish nodules occurring predominantly on the exposed surfaces and from which, on puncture, a gelatinous, translucent, yellowish or brownish material can be expressed. Microscopically, hyalin-like degeneration of the collagen bundles of the dermis is found. To our knowledge, about 50 authentic cases have been reported in the literature. According to Jager,[1] who tabulated all reports of cases up to 1925, the first case was reported by Wagner in 1866. Besnier and Balzer recognized the disease as arising from the connective tissue of the dermis. Besnier [2] named it "colloid degeneration of the skin." The most recent, and one of the few articles in the American literature, was by Labadie,[3] in August 1926. He reported 1 case and reviewed some 20 previously reported. The accompanying table includes all cases reported since the tabulation by Jager.[1]

REPORT OF A CASE

Mrs. S. A. K., aged 75, consulted one of us (M. J. R.) because of numerous "growths" on her skin. The early lesions had appeared some five years previously as small pink growths, 0.5 cm. in diameter, on the chest. They had slowly increased in size, and new ones had continued to appear on other parts of the body. The early lesions were firm, but as they enlarged they became soft and changed in color from pink to orange. They caused no discomfort. The patient had always enjoyed excellent health, diphtheria in childhood being her only past illness. She had had no operations.

Examination showed an elderly gray-haired woman who appeared to be in excellent health despite her advanced age. Distributed over the trunk, arms, thighs

1. Jager, T.: So-Called Colloid Degeneration of the Skin, Arch. Dermat. & Syph. **12**:629 (Nov.) 1925.

2. Balzer, E.: Sur un cas de dégénérescence colloïde du derme, affection non décrite, non dénommée ou improprement dénommée colloid-milium, Ann. de dermat. et syph. **10**:461, 1879-1880.

3. Labadie, J. H.: Colloid Degeneration of the Skin, Arch. Dermat. & Syph. **16**:156 (Aug.) 1927.

Cases of Colloid Degeneration of the Skin Reported Since the Tabulation by Jager [1]

Author	Age of Patient	Sex	Age at Onset	Distribution of Lesions	Reference
Johnston, L., and Johnston, P. N.	(1) ?	?	?	Dorsal surface of hands	M. J. Australia **1**: 304, 1916
	(2) 37	♂	30	Face, neck, forearms and hands	
Ruedemann, R., Jr.	36	♀	32	Left cheek	Arch. Dermat. & Syph. **5**: 951 (May) 1922
Dubreuilh, W.	43	♂	37	Cheeks and back of hand	Bull. Soc. franç. de dermat. et syph. **10**: 515, 1922
Mook, W. H.	17	♀	15	Neck	Arch. Dermat. & Syph. **11**: 709 (May) 1925
Greenwood	38	♂	37	Eyelids, face, neck and flexures of arms	Arch. Dermat. & Syph. **13**: 421 (March) 1926
Werther	70	♂	?	Forehead, eyebrows and nose	Zentralbl. f. Haut- u. Geschlechtskr. **22**: 619, 1927
	63	?	?	Eyebrows and forehead	Zentralbl. f. Haut- u. Geschlechtskr. **23**: 29, 1927
Pineda, and Sanz de Grado	?	?	?	Around eyes and nose	Rev. españ. de urol. y dermat. **28**: 239, 1926; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **23**: 90, 1927
Davies, J. H. T.	45	♀	35	Eyelids and forehead	Proc. Roy. Coll. Med. **20**: 75, 1927
Labadie, J. H.	47	♀	32	Plaque on forehead	Arch. Dermat. & Syph. **16**: 156 (Aug.) 1927
Arnold, A. C.	29	♂	25	Backs of hands	M. J. Australia **1**: 241, 1928
Engman, M. F.	32	♀	5	Neck, face and chest	Arch. Dermat. & Syph. **18**: 459 (Sept.) 1928
Fukai, A.	45	♂	?	Forehead, cheeks, nose and eyelids	Acta dermat. **11**: 123, 1928; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **28**: 168, 1928
	56	♂	?	Face and back of hands	
Morrow, H.; Miller, H., and Taussig, W.	?	?	?	Dorsum of hand	Arch. Dermat. & Syph. **21**: 689 (April) 1930
Navarro, M. A., and Aguilera, C.	68	♀	65	Forehead, cheeks and backs of hands	Actas dermo-sif. **22**: 728, 1930; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **38**: 101, 1931
Cholnoky, L.	51	♀	?	Forehead, nose and both sides of face	Zentralbl. f. Haut- u. Geschlechtskr. **41**: 426, 1932
McLeod, J. M. H.; Wigley, J. E. M. and Muende, I.	50	♂	48	Backs of hands	Brit. J. Dermat. **44**: 257, 1932
Truffi, G.	(1) ?	?	?	Hands	Boll. sez. reg. Soc. ital. di dermat. **4**: 202, 1932; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **46**: 489, 1933
	(2) ?	?	?	Hands and face	
Monacelli, M.	42	♀	30	Face and back of hand	Ann. de dermat. et syph. **5**: 29, 1934
Bejarana, J.	(1) (young)	♂	?	Face	Actas dermo-sif. **26**: 1123, 1934; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **50**: 481, 1935
a (?)	(2) (young)	♂	?	Nose and about mouth	
	(3) ?	?	?	Back of hand	Actas dermo-sif. **27**: 524, 1935; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **51**: 487, 1935
Casazza, R.	50	♂	?	?	Boll. sez. reg. Soc. ital. di dermat. **2**: 166, 1936; abstracted, Zentralbl. f. Haut- u. Geschlechtskr. **55**: 141, 1937
Chambers, S.; Anderson, N. P., and Rosenberg, M. W.	56	♂	53	Hands and back of neck	Arch. Dermat. & Syph. **35**: 1167 (June) 1937
Photinos, G., and Petropoulos	56	♀	?	?	Zentralbl. f. Haut- u. Geschlechtskr. **59**: 117, 1938
Spilman, L.; Watrin, J., and Weille, J.	58	♀	57	Face, hands and forearms	Bull. Soc. franç. de dermat. et syph. **45**: 535, 1938
Oliver, E. A., and Gold, M. A.	62	♂	58	Forehead	Arch. Dermat. & Syph. **44**: 302 (Aug.) 1941
Way, S. C.[13]	45	♂	33	Face and hands	Arch. Dermat. & Syph. **45**: 1148 (June) 1942

and legs were numerous pink papules and orange nodules and plaques (fig. 1). The small papules were elevated and firm. A few of the larger plaques were firm, but the majority were oval, flattened, soft and pliable and were covered with atrophic, cigaret-paper-like skin, which could be readily picked up with the fingers. A striking clinical feature of the larger lesions was their orange color. When the surface was incised, a yellowish gelatinous fluid exuded, which stained gauze yellow. The largest plaques on the abdomen measured 2.5 by 3 cm. A lesion on the upper left side of the chest and one on the upper part of the back were

Fig. 1.—The small plaques are firm and pink and the larger ones orange-yellow and soft.

deep red with superficial sanguineous crusting, presumably from hemorrhage due to trauma. On the upper part of the back were several large brownish black seborrheic keratoses; many small lesions of the same type were present on the abdomen.

General physical examination revealed no abnormalities. A complete blood count was essentially normal, and the urine was normal. Serologic reactions for syphilis were negative. Determinations of blood sugar on two occasions showed 137 and 133 mg. per hundred cubic centimeters. The blood cholesterol content

was 240 mg. per hundred cubic centimeters. Blood cholesterol esters were 164 mg. per hundred cubic centimeters. The patient was considered by Dr. William Jermain, the medical consultant, to have borderline diabetes. She was given a diet of 1,500 calories, consisting of 125 Gm. of carbohydrate, 50 Gm. of protein and 90 Gm. of fat.

Two biopsies were made, one of a specimen from a recent lesion on the left side of the chest, and the other of a specimen from an atrophic lesion on the lower part of the abdomen. These observations were made on microscopic

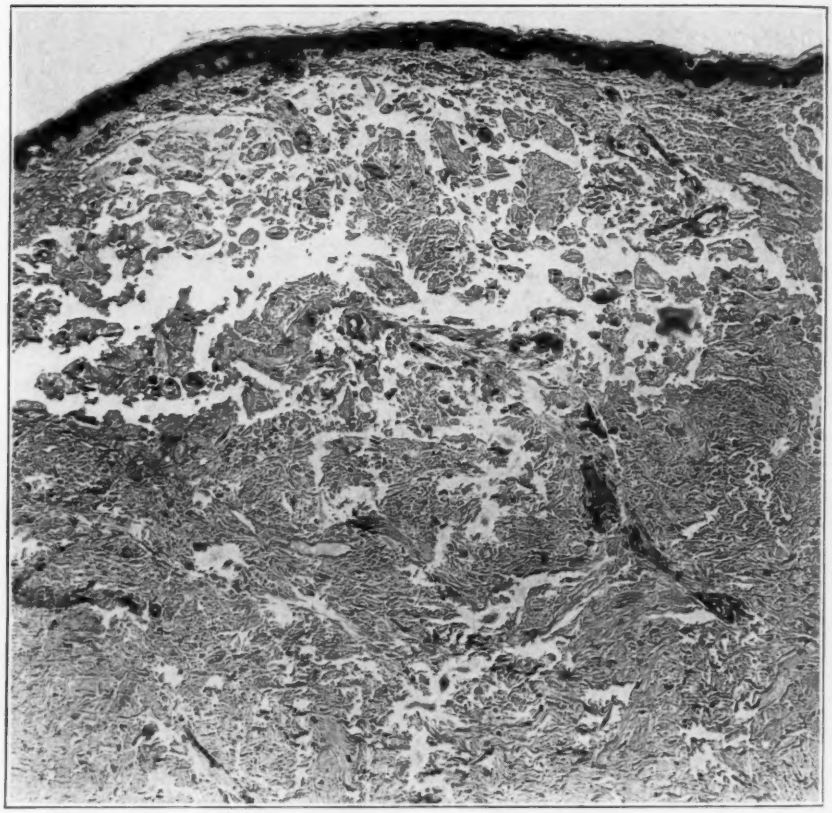

Fig. 2.—Low power photomicrograph showing extensive degeneration of collagen (hemalum, erythrosin and saffron stain).

examination: A section from a recently developed lesion, stained with hemalum, erythrosin and saffron, showed a thin epidermis with a thin layer of normal collagen just within. The collagen throughout the section appeared for the most part swollen, with fibers often separated as if by a fluid substance, and there was a little pink-staining coagulated material in the interstices (fig. 2). The degenerated collagen took a pink stain. Nuclei were sparsely distributed throughout the degenerated collagen, and no sign of necrosis was seen. About some of the blood vessels there was a thin layer of normal collagen. Deeper in the section

there was a progressive increase in the percentage of normal collagen, although even deep in the dermis about half of it had degenerated. No normal follicles or sweat gland ducts were evident. A stain for elastic fibers showed a few normal fibers in association with the normal collagen deeper in the section. They were also in evidence about the larger blood vessels. In the areas of greatest degeneration, elastic fibers were seen coursing in several directions, many of them being short, as though the fibers had broken up into small oval and round segments.

A section from a lesion of longer duration showed essentially the same picture, although there were some homogeneous masses containing practically no nuclei.

Special stains for collastin and collacin did not show any of these substances. A frozen section stained with scarlet red showed diffuse staining of some of the collagen bundles with what appeared to be fine fat droplets between the fibers. There was no evidence of lipid-containing histiocytes.

Some three years after these observations were recorded the patient was reexamined. At this time it was noted that none of the original lesions had disappeared. Several had increased in size, and there were a few new papules and nodules. A solitary lesion on the left side of the breast had cleared in the center, leaving a normal-appearing epidermis surrounded by an orange rim.

Several lesions on the lower part of the abdomen and one on the left arm had undergone striking changes, forming bladder-like projections similar, except for color and size, to those seen in the type of cutaneous atrophy described by Schweninger and Buzzi.

Further biopsies were performed at this time, but the histologic picture was essentially the same as on previous examinations.

PATHOLOGY

McCarthy [4] stated:

> Histologic studies have shown that the disease is in no way connected with the surface or glandular epithelium and that it is a degeneration of the collagenous portion of the connective tissue of the cutis. . . . Upon histological examination we are immediately interested by the presence of large, nodular masses lying just under the epithelium and extending to the level of the sebaceous glands. . . . . These nodules appear as peculiar, homogeneous or coarsely bundled masses very poor in cellular elements. . . . Curiously enough, these bundles in general run in a direction contrary to that which we would expect for they are usually seen at right angles to the surface epithelium. . . . According to Gans, the walls of the larger vessels are also involved in this degeneration; their elastica has disappeared and the vessel wall is represented by a broad thick band of hyalinized tissue.

The designation colloid is used for several substances which present physical similarities, the chemical natures of which, however, are still somewhat of a mystery. Colloid means gluelike; the designation is applied to transparent, homogeneous, semisolid substances of both epithelial and connective tissue origin. A representative of epithelial colloid is that present in the thyroid gland.

4. McCarthy, L.: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931.

In the case of the connective tissue, two types of degeneration occur, which are apparently closely related, namely, hyalin and colloid. McCarthy stated that "in the past the terms 'hyaline' and 'colloid' were synonymous for a certain type of degeneration of the skin." In regard to the former, Mallory [5] stated: "The collagen fibrils of connective tissue are often under certain conditions rendered invisible, as they usually are in cartilage and bone, and probably in the same way, by the deposition of a homogeneous substance between them, which binds them intimately." The collagen fibers are thus transformed into coarse, homogeneous, thickened bundles.

In discussing the chemistry of hyalin, Wells [6] stated that connective tissue hyalin is deposited in or among the fibrillar substance of connective tissue but that there are undoubtedly several different sorts of chemical substances responsible for various forms of connective tissue hyalin. Some are related to amyloid, and some represent collagen which has become changed physically rather than chemically. Schmorl [7] stated that von Recklinghausen designated as hyalin several substances which are translucent, shiny and insoluble in water, alcohol, weak acids and bases but soluble in strong potassium hydroxide and hydrochloric acid. They may be stained with acid aniline dyes. He recommended Weigert's fibrin stain, which colors hyalin blue to violet, Van Gieson's method, by which hyalin is stained bright red or orange, and Russel's carbolfuchsin method, whereby the hyalin is stained bright red. Gans [8] stated that hyalin or colloid designates not a chemically characteristic entity but rather a group of protein modifications with similar optical characteristics.

Weidman [9] considered colloid degeneration "a (soft) variation of hyaline degeneration, modified or not by secondary (incomplete) liquefactive or at least softening changes akin to those of connective tissue mucin (paramucin)." He attributed the yellow color of the nodules to a more or less fortuitous fatty degeneration. McCarthy cited Arzt as stating the belief that both the collagenous and the elastic tissues are involved in the degeneration, a concept advanced by Unna in 1894. Weidman supported this concept by stating that forms morphologically those of both elastic fibers and collagen bundles are frequently affected by the

5. Mallory, F. B.: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, 1914.

6. Wells, H. G.: Chemical Pathology, Philadelphia, W. B. Saunders Company, 1925.

7. Schmorl, G.: Die pathologisch-histologischen Untersuchungsmethoden, Leipzig, F. C. W. Vogel, 1925.

8. Gans, O.: Die allgemeine pathologische Anatomie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 4, pt. 3.

9. Weidman, F. D.: The Pathology of the Yellowing Dermatoses, Arch. Dermat. & Syph. **24**:954 (Dec.) 1931.

same retrogressive circumstances and that under these circumstances elastic fibers appear to take on to a greater or lesser extent the morphologic characteristics of collagen bundles and vice versa. He therefore concluded that the condition cannot be classified strictly as an "elastosis" or "collagenosis." On the other hand, Schmidt,[10] Reizenstein [11] and Kreibich [12] stated that colloid arises solely from elastic fibers.

In regard to the chemistry of colloid, Wells [6] stated:

> It would seem that the safest view to take is that *the word colloid is merely morphologically and macroscopically descriptive* of certain products of cell activity or disintegration, which have nothing in common except the fact that they form a thick, glue-like or gelatinous, often yellowish or brownish substance. *There is no one definite substance colloid,* according to the usual usage of the word in pathological literature, but many different protein substances may assume the appearance to which the name "colloid" is given.

Jager [1] performed various chemical tests on the material expressed from the lesions occurring in colloid degeneration of the skin. He found it to be insoluble in water, acetic acid and alcohol. It dissolves slowly in a tenth-normal solution of sodium hydroxide, leaving a fine network of connective tissue, in which each colloid mass seems to be enveloped. The dissolved material could not be precipitated by acetic acid or alcohol. Reactions to chemical tests for pseudomucin and amyloid were negative.

Staining methods give less assistance in identification of colloid than is the case with hyalin. In tissue stained by Van Gieson's method, colloid tends to stain with trinitrophenol (picric acid) rather than with fuchsin, as does hyalin. According to Jager,[1] Ernst's method of differentiation of the two substances on this basis has been shown to be incorrect by van Kalden and others. While this method usually permits accurate differentiation, the indefinite chemical nature of both hyalin and colloid would scarcely be expected to permit of positive tinctorial identification.

Labadie [3] stated the belief that the disease is a clinical entity, best classified under the simple degenerations.

ETIOLOGY

The cause of colloid degeneration is unknown. The majority of patients are men over 40 years of age. Exposure to sunlight, heat and the elements have been emphasized as possible factors, since the disease occurs predominantly on the exposed surfaces and because most of the

10. Schmidt, M. B.: Ueber die Altersveränderungen der elastischen Fasern in der Haut, Arch. f. path. Anat. u. Physiol. **125**:239, 1891.

11. Reizenstein, A.: Ueber die Altersveränderungen der elastischen Fasern in der Haut, Monatsh. f. prakt. Dermat. **18**:1 (Jan.) 1894.

12. Kreibich, C.: Ueber Bindegewebsdegeneration, Arch. f. Dermat. u. Syph. **130**:535, 1921.

cases have been reported from warm or temperate climates. Jager [1] and others have reported aggravation and extension of the disease during the summer months. Jager stated:

> It seems probable that the disease is due to a congenital dystrophy of the skin, as suggested by some of the Italian writers, especially Bosselini, in which the afflicted person is peculiarly susceptible to direct sunlight and heat. . . . The early age at which the disease first makes its appearance, and especially its occurrence in two members of the same family, as recorded by Bosselini, seem to be in harmony with this view.

It is difficult to reconcile this statement with the fact that a familial tendency has practically never been noted and that the majority of patients have been beyond middle life at the onset of the disease. The appearance in our patient of many lesions limited to the covered portions of the body would seem to indicate that exposure to the elements, while possibly contributing in many instances, is not absolutely necessary for the production of colloid degeneration. Way [13] reported vitamin C deficiency in his case with improvement following its attempted correction.

DIAGNOSIS

Because of the striking orange color of the lesions in our case, we immediately thought of one of the cutaneous lipoidoses, such as xanthoma, as a probable diagnosis. This diagnosis was immediately discarded on microscopic examination of sections stained to demonstrate fat, since very little was found. Xanthomatous and other lipoid tumors of the skin, such as those of extracellular cholesterosis (Urbach) and lipid proteinosis (Urbach), are usually hard, yellowish plaques or nodules which have a characteristic microscopic picture entirely unlike that found in colloid degeneration of the skin. Frequently there is alteration of the blood lipids. Because the lesions of pseudoxanthoma elasticum are characterized by a yellowish color, this disease also is considered in the differential diagnosis. This rare condition is characterized by small flat yellowish nodules on the neck, trunk and flexor surfaces about the joints. Microscopically clumping and splitting of elastic fibers, which are increased in number, are seen in the subpapillary layer.

Necrobiosis lipoidica diabeticorum is characterized first by small circinate, oval or irregular, flesh-colored, pink or yellowish nodules, usually situated on the lower extremities. Later, the center becomes depressed, due to loss of tissue, and eventually a depressed atrophic scar is produced. Microscopic examination shows first inflammation of the deeper vessels, in the walls of which lipids are deposited and about which is a lymphocytic infiltrate. The collagen bundles are swollen and infiltrated with lipoid material. Necrosis occurs in the center of the

13. Way, S. C.: Colloid Milium, Arch. Dermat. & Syph. **45**:1148 (June) 1942.

lesion. The patients are usually diabetic, although occasionally non-diabetic patients with this disease have been reported on.

In senile elastosis the skin appears yellowish, pasty and thick, but there is no tumor formation. Microscopically the alteration is predominantly in the elastic tissue, which is hyperplastic, not unlike the histologic picture in pseudoxanthoma elasticum.

The term elastoma usually refers to a connective tissue tumor arising from malformations of the mesodermal layer. The nodular lesions are usually smooth and slightly rounded or flat, yellowish and of a rubbery consistency. In this disease no thick glairy material can be expressed on puncture of the lesions and the histologic picture is entirely unlike that either described or pictured under the name of colloid degeneration of the skin. The only similarity seems to be in the yellowish color and rubber-like consistency.

Sarcoids and rare tumors of the skin, such as lymphocytomas, might be considered in the differential diagnosis, but here again the microscopic pictures are characteristic.

COMMENT

The individual plaques in our case correspond clinically with those described in colloid degeneration of the usual variety, namely, those on the exposed surfaces. The gelatinous fluid which escaped when the lesions were punctured and stained the gauze yellow is also in accordance with the aforementioned diagnosis. While the patient was considered to have mild diabetes, absence of necrosis on microscopic examination is against the diagnosis of necrobiosis lipoidica diabeticorum. We could find no mention of diabetes in the reported case histories of colloid degeneration, although Monacelli and Casazza, whose cases are included in the table, mentioned the presence of hypercholesteremia, which was also present in our case. The advanced age of our patient would favor a degenerative process, although in most reported cases of colloid degeneration the patients were considerably younger. The microscopic picture in our case differs from that usually seen in colloid degeneration in that instead of there being small areas of degenerated collagen corresponding to the clinical nodules seen in the ordinary case, the entire plaque showed uniform, superficial, collagenous degeneration. Practically all the superficial fibers of collagen had undergone degenerative changes, which process extended to the deeper end of the section in decreasing degree. The homogeneous solid nature of the colloid in the usual case may be due to the compression by more or less normal surrounding connective tissue. In our case the lesions were elevated above the level of the skin and not under tension, so that the colloid material was less compressed. We are led to conclude, therefore, that the disease described by us constitutes an unusual form of collagen degeneration and is best included under the title colloid degeneration.

SUMMARY

About 50 cases of colloid degeneration of the skin have been reported since 1866. A table of cases supplementing that of Jager, published in 1925, is presented.

The distribution of the lesions is predominantly on exposed surfaces; exposure to the elements is considered as one of the causes.

Colloid is a physical rather than a chemical designation. The causes for its formation are not necessarily always the same. It may arise from collagen or elastin or both.

The case of a mildly diabetic patient with multiple bright orange plaques on covered portions of the body is reported; microscopic section showed extensive collagen degeneration.

Hypercholesteremia, present in our patient, has been mentioned in only 2 other cases, in both of which there was colloid degeneration of the skin of exposed areas only.

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ORIENTAL SORE IN THE UNITED STATES

REPORT OF A CASE

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Oriental sore (cutaneous leishmaniasis) is seldom seen in the United States. In the case reported in this paper, although the disease was contracted in Greece, lesions were first manifested after the patient had returned to New York. The eruption resembled cutaneous tuberculosis.

REPORT OF CASE

History.—J. D.,[1] a man aged 48, born in Greece, registered at the Skin and Cancer Unit on March 20, 1941, complaining of an eruption of eighteen months' duration. Until the onset of his present illness he had always enjoyed good health, except for a chronic otitis media and mastoiditis on the right side of fifteen years' duration. He has lived in the United States for twenty years but has revisited Greece on several occasions. The last visit was in 1938-1939. At that time the patient was frequently bitten by sandflies.

The first lesion appeared on the forehead a few months after his return from Greece. A few weeks later a nodule appeared on the extensor surface of the right wrist, and six months later the patient noticed an involvement of the right ear lobe. These three lesions were still present at the time of the first visit to the clinic. A nodule appeared on the extensor surface of the left hand shortly after the ear lobe became involved, but this lesion disappeared spontaneously in three months.

Description of Eruption on First Visit to the Clinic.—In the middle of the lower part of the forehead just above the glabella there was a dull red, extremely hard nodule, measuring 1.5 by 1 cm. A tightly adherent, narrow, thin crust 0.25 cm. long was seen at the crest of the lesion. The right ear lobe was dusky red, about three times its normal size and intensely indurated. The dependent surface of the lobe was covered with a tightly adherent, verrucous crust. The skin of the remainder of the ear lobe was tense and thin. On the dorsum of the right wrist there was a lesion similar to the one on the forehead. When the crusts were forcibly removed from these lesions, superficially eroded areas were revealed, and a drop of serum could, with difficulty, be expressed from these

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1. This case was presented before the New York Academy of Medicine, Section of Dermatology and Syphilis on April 1, 1941 (Arch. Dermat. & Syph. **44:** 1120 [Dec.] 1941) by Dr. Henry D. Niles.

areas. On the dorsum of the left hand there was a smooth, barely visible, brown scar. There were no subjective symptoms.

Laboratory Report.—A smear of the serum expressed from the lesion on the right ear lobe, stained with Giemsa's stain, showed a few monocytes containing bodies suggestive of Leishmania tropica but not definitely identifiable as such.

Histologic examination [2] of the lesion on the hand showed the following features: The epidermis was normal. In the cutis there were many nodes composed of lymphocytes and epithelioid cells. An occasional huge foreign body

Fig. 1.—Cutaneous leishmaniasis (resembling sarcoid) involving the dorsum of the hand.

giant cell was noted. Within the nodes the connective tissue had undergone degenerative changes. The nodes were not sharply outlined and did not have a perivascular distribution. No leishmania bodies were found.

Histologic examination [2] of the lesion on the ear showed the following features. The stratum corneum was thickened and contained many parakeratotic

2. The tissue for histologic examination, both from the hand and from the ear lobe, was excised before roentgen treatment was administered.

cells. It was covered by serosanguinous exudate. The epidermis was moderately acanthotic except for a few areas in which pseudoepitheliomatous hyperplasia was noted. The cutis was densely infiltrated by lymphocytes, epithelioid cells, plasma cells and many irregularly oval, pale cells, each with a single nucleus. In the cytoplasm of each of these last-mentioned cells about twenty-five leishmania bodies were seen. Each of these organisms had a small, deeply staining,

Fig. 2.—Cutaneous leishmaniasis (resembling lupus tumidus) involving the ear lobe.

central nucleus and was surrounded by a narrow, pale zone of clear protoplasm. An occasional foreign body giant cell was observed.

The Wassermann and Kahn reactions of the blood were negative. The results of graded intradermal tuberculin tests were within normal limits. Roentgenologic examination revealed no abnormalities in the lungs or long bones. Cultures and smears for lepra bacilli and smears for tubercle bacilli revealed no organisms. Cultures and potassium hydroxide preparations showed no fungi.

Course.—No treatment was undertaken until April 17, one month after the patient first came to the clinic. During this period no change was visible in the eruption. On April 17, before a diagnosis had been established, the three active lesions were each treated with ¾ erythema dose of roentgen rays (366 r), filtered through 3 mm. of aluminum. Two weeks later the same treatment was applied to the lesion on the forehead. On May 18 the final diagnosis was established by the finding on histologic examination of Leishmania tropica in

Fig. 3.—Histologic section from the ear lobe showing numerous leishmania bodies in a large monocyte (× 3,700; hematoxylin and eosin).

the tissue from the ear. Between May 20 and July 2 thirty intravenous injections of 5 cc. each of a 1 per cent solution of antimony and potassium tartrate were administered. Because of the patient's complaint of severe pain in the joints, the injections were thereafter given every other day instead of four or five times a week. Forty-one injections in all were given. By the end of July the three lesions had undergone involution, and by October only smooth pigmented scars marked the sites of the lesions on the forehead and wrist. The ear lobe was slightly indurated but had returned to its normal size and color.

COMMENT

Cases of oriental sore are seldom reported in the United States, and it is possible that a certain number of them escape recognition. The disease is always contracted abroad in areas where it is endemic. Our patient did not have visible lesions until after his return to the United States, an occurrence made possible by the incubation period, which varies from a few weeks to more than a year. Lambert [3] reported similar observations and warned against the possibility of unrecognized cases in the United States becoming the source of infection for other cases. However, there is no record of such an occurrence. Templeton [4] described a patient who was experimentally inoculated with cutaneous leishmaniasis in Beirut, Syria; the lesion developed four months later in England [5] and the patient was subsequently seen by Templeton in the United States. In a recent article reporting 4 cases of oriental sore, Dwork suggested that the condition may be seen here more frequently in the future because of the return of expeditionary forces from areas where the disease is endemic.[6]

The clinical picture of this disease may deviate from the classic description of oriental boil; in fact, it is doubtful that this term is truly descriptive. Fox [7] said, in discussing Trow's case: "The term Aleppo boil is a poor one, as the disease does not resemble a furuncle but rather simulates a crusted impetiginous or echthymatiform eruption." Our case, like many described in the literature,[8] might have been mistaken for one of cutaneous tuberculosis, the lesion on the ear resembling lupus tumidus while the lesions on the forehead and hand resembled sarcoid. The lesions were harder to the touch than would be expected in tuberculosis, and the central crust in the sarcoid-like lesions made that diagnosis doubtful. The histologic examination of the nodule on the right wrist showed a tuberculoid structure without Donovan bodies, while these organisms were found in great numbers in the tissue from the ear lobe. It is a common experience to find the older lesions apparently devoid of Leishmania tropica, while this causative agent can readily be demonstrated in more recently developed nodules in the same patient.

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3. Lambert, R. A.: Oriental Sore (Cutaneous Leishmaniasis) in the United States, J. A. M. A. **80**:986 (April 7) 1923.

4. Templeton, H. J.: Cutaneous Leishmaniasis, Experimentally Produced, California & West. Med. **54**:70 (Feb.) 1941.

5. Templeton, H. J.: Personal communication to the authors.

6. Dwork, K. G.: Cutaneous Leishmaniasis (Oriental Sore) in the United States and Canada, Arch. Dermat. & Syph. **45**:676 (April) 1942.

7. Fox, H., in discussion on Trow, E. J.: Oriental Sore, Arch. Dermat. & Syph. **35**:455 (March) 1937.

8. Mayer, M., and Nauch, E. G., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pt. 1, p. 119.

In classification of the disease in this case with the tuberculoid group it must be separated from those forms recently described as leishmaniasis recidiva cutis.[9] In the latter condition nodules resembling lupus vulgaris appear in and near the scars of a preexisting primary leishmania infection. In our case the eruption was the primary eruption and resembled tuberculosis only clinically and to some extent histologically.

Finally, the fact that individual lesions as well as the entire eruption lasted for more than a year in this case is to be noted. Many cases of cutaneous leishmaniasis of the eastern hemisphere of long duration have been described, but the customary conception of the disease is that it disappears in less than a year.

SUMMARY

1. A case of oriental sore developing in the United States is described.

2. Leishmania tropica was demonstrated on histologic examination.

3. The case is unusual in that: (*a*) The lesions first developed after the patient returned to the United States; (*b*) the lesions resembled cutaneous tuberculosis, and (*c*) the eruption persisted for more than eighteen months.

2 West Eighty-Seventh Street.

9. Berlin, C.: Leishmaniasis Recidiva Cutis: Leishmanid, Arch. Dermat. & Syph. **41**:874 (May) 1940.

A TRANSPARENCY TEST FOR THE DIFFERENTIAL DIAGNOSIS OF PLANTAR WARTS

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In most instances it is easy to recognize plantar warts by inspection. The majority of plantar warts are found chiefly on points of pressure and friction and so are often complicated with clavi and calluses. Sometimes the plantar wart is so covered with keratin that its true identity is missed. Shaving off bits of hyperkeratotic material may help in the diagnosis and also serve, of course, as a therapeutic aid. But certain forms of complicating clavi are not seen any more clearly with shaving, and often this shaving is painful.

The various hyperkeratotic lesions on the sole or even on the palm are rendered clearer for observation by the application of such a material as alcohol, xylene or oil, which makes the keratin transparent. This is due to penetration of the keratin by the material used and reflection of light through a medium now showing approximately the same index of refraction. A strong light helps considerably. This light may be held at the side and so bring about lateral transillumination of the lesion, or it may be held directly over the hyperkeratotic mass. The normal skin under such conditions shows stratification with alternating ridges and depressions. In the case of a callus, the color is more yellowish, some of the ridges are flattened and separated and brownish waxlike spots may be found scattered deep in between the changed ridges. These brownish spots represent chemical changes in the keratin and may be changes productive of a more waxy substance. As a rule, no points of tenderness can be established over these brownish spots.

In the case of a clavus, which is really a more highly developed callus, the points of maximum pressure become changed and localized centrally so that the lesion resembles an eye and has been called a "chicken eye." With the transparency test such a clear, waxy, brownish "eye" shows no ridges at all. A heavy whitish rim may be seen around the lesion. Since the central portion extends directly to the corium, there is definite point tenderness. Moreover, tiny black spots, representing bits of coagulated blood, may be found scattered through this "eye." Likewise, there are no ridges visible around the rim, nor is there any point of tenderness over it. Frequently there may be associated

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periosteal tenderness, and this may be detected by pushing the entire lesion to the side and then palpating deeply for tenderness of bone.

On the plantar surface the usual small amount of interpapillary keratinization of the wart is replaced by a tremendous degree of keratosis, which may extend even over the top of the wart. With the transparency test one recognizes the papillomatous projections (areas of acanthosis) of the wart in the form of discrete circular plugs which may be embedded deep in the lesion. These plugs are separated by bits of black dirt, outlining the top portions of the papillomatous plugs. After keratinization covers these plugs completely, these dirt rims are not seen. Blackish spots, representing bits of coagulated blood from the corium, may be found scattered through the keratin between the plugs and also in the plug itself. As aforementioned, these deep, blackish points alone are not diagnostic of plantar warts.

The transparency test may also be used to follow the results of local treatment, since the scar tissue may also be rendered transparent or even translucent and reforming wart plugs or even reforming waxy areas of clavi and calluses may be detected early.

CONCLUSIONS

A plantar wart which is usually recognized with ease, may be difficult to detect when complicated with a clavus or callus, even when the hyperkeratotic areas are trimmed down. With the use of a strong light and a material such as alcohol, xylene or oil, the lesion will become transparent and its true identity established. The simple transparency test may be used also to detect possible recurrences after local cauterization.

BIOLOGIC FALSE POSITIVE REACTIONS FOR SYPHILIS ASSOCIATED WITH HYPERPROTEINEMIA

PRELIMINARY REPORT

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The problem of the false positive reaction to a serologic test for syphilis is of great importance, especially with the advent of routine serologic tests in premarital examinations and selective service examinations and in connection with the antisyphilis campaign of the United States Public Health Service.

A false positive reaction may be either technical (due to laboratory variations) or biologic. The biologic type of false positive reaction is rarely encountered in normal persons (1 in 4,000); when it does occur it is thought to be due to the presence of a reagin-like substance which has recently been isolated from lower animals.[1]

This report is concerned with the more frequent type of biologic false positive reaction, that which has been reported for persons with diseases other than syphilis, viz., yaws (100 per cent), leprosy (40 to 80 per cent), malaria (100 per cent at some time during the infection) and

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1. Moore, J. E.; Eagle, H., and Mohr, C. F.: Biologic False Positive Serologic Tests for Syphilis: III. A Suggested Method of Approach to Their Clinical Study, J. A. M. A. **115**:1602-1606 (Nov. 9) 1940.

infectious mononucleosis and less frequently pneumonia, acute infections of the upper respiratory tract, vaccinia and scarlet fever.[2] The questions at issue are: 1. What is the mechanism of the biologic false positive reaction? 2. How can the false positive reaction be recognized?

The question of the mechanism of this biologic false positive reaction has been the object of considerable thought and investigation. Alteration in the blood cholesterol and blood lipid content has been mentioned as playing a role, especially in conditions in which the values for these substances are elevated, as in pregnancy and jaundice. In these conditions the false positive reactions usually occur in response to the Wassermann test with the cholesterolized antigen.

Evidence has been presented that alterations in the blood globulins are concerned in the reactions to flocculation and complement fixation tests for syphilis and also in the nonspecific (false) positive and anticomplementary reactions. Kolmer[3] said: "While the globulins of syphilitic serum are strongly suspected of being concerned in these processes, their relation is not clear." And again (after discussing the experimental evidence for the relative roles of lipids and globulins in these reactions): "It is highly probable that the anti-lysins of human and other sera are identified with the protein fractions under certain circumstances and with the lipoids in others." Ether anesthesia, acetic acid poisoning and even sulfanilamide and its derivatives have been suggested as possible causes for false reactions.

Moore, Eagle and Mohr[1] have outlined clinical and laboratory procedures that may be instituted when the biologic false positive reaction is suspected; among these are suggested the careful study of blood smears for malaria, the Paul Bunnel test for infectious mononucleosis and the determination of the sedimentation rate. Regarding the last-mentioned measure they stated: "A greatly increased sedimentation rate observed during an acute illness, which is accompanied by positive serologic tests for syphilis but which tends spontaneously to fall toward normal as acute symptoms subside, speaks moderately in favor of a biologic false positive serologic reaction."

Kahn[4] has recently suggested the use of a verification test to differentiate the true from the false positive reaction. This test depends on his observation that the true reaction is strongest at 37 C, and diminished or absent at ice box temperatures, while the reverse is true of the false reaction. The validity of this test remains to be determined, and it has not as yet been generally accepted.

2. Mohr, C. F.: Biologic False Positive Tests for Syphilis, editorial, Ann. Int. Med. **14**:171 (July) 1940.

3. Kolmer, J. A.: Infection, Immunity, and Biologic Therapy, ed. 3, Philadelphia, W. B. Saunders Company, 1925, pp. 584 and 436.

4. Kahn, R. L.: False Positive Reactions, Univ. Hosp. Bull., Ann Arbor **6**:26-27 (April) 1940.

Hyperproteinemia (except when caused by dehydration) has been known to be associated almost invariably with highly elevated sedimentation rates, even in the absence of fever.[5] It has also been observed that anticomplementary Wassermann reactions are frequently associated with hyperproteinemia, especially in patients with such conditions as

TABLE 1.—*Comparison of Conditions Reported to Be Associated with Hyperproteinemia with Conditions Reported to Give Biologic False Positive Serologic Reactions and Anticomplementary Wassermann Reactions (from a Review of the Literature)*

Hyperproteinemia *	Biologic False Positive Serologic Reaction †	Anticomplementary Wassermann Reaction ‡
Lymphogranuloma venereum	Lymphogranuloma venereum	Lymphogranuloma venereum
Endocarditis lenta	Endocarditis lenta	Endocarditis lenta
Multiple myeloma		Multiple myeloma
Leishmaniasis	Leishmaniasis	Leishmaniasis
Cirrhosis of the liver	(Jaundice)	Cirrhosis of the liver
Tuberculosis	Tuberculosis	Tuberculous lymphadenitis
Malaria	Malaria	
	Pregnancy	Pregnancy
Pneumonia	Pneumonia	
Scarlet fever	Scarlet fever	
Leprosy	Leprosy	
Trypanosomiasis	Trypanosomiasis	
Sarcoid of Boeck	Sarcoid of Boeck	
		Lymphosarcoma
	Weil's disease	
	Yaws	
	Infections of the upper respiratory tract	
	Vincent's infections	
	Glanders	
	Chancroid	
	Typhus fever	
	Infectious mononucleosis	
	Rat bite fever	
	Vaccinia	
	Injections of horse serum	
	Malignancy	
	Rheumatic fever	
	Uremia	

* Shuman, H. H., and Jeghers, H.: The Value of Routine Blood-Protein Determinations: Report of Results in Three Hundred and Twenty Consecutive Cases, New England J. Med. **222**: 335-339 (Feb. 29) 1940. Peters, J. P., and Eisenman, A. J.: Serum Proteins in Diseases Not Primarily Affecting Cardiovascular System or Kidneys, Am. J. M. Sc. **186**: 808-833 (Dec.) 1933.

† Moore, Eagle and Mohr.[4] Editorial.[2] Kolmer.[3]

‡ Cardon, Atlas and others.[7] Gutman, A. B., and Williams, R. D.: Anti-Complementary Wassermann Reactions Associated with Hyperproteinemia, J. Clin. Investigation **15**: 458 (July) 1936. Mu and Huie, cited by Gutman and Williams.

lymphogranuloma venereum and multiple myeloma.[5] A comparison of the conditions reported with hyperproteinemia with those conditions reported to give biologic false positive or anticomplementary reactions (table 1) suggests that perhaps a common factor is concerned.

One of us (L. C.) had a case under observation which illustrates this point: A 21 year old white man after surgical removal of a gangrenous appendix became free of fever within five days. He remained so until

5. Jeghers, H., and Selesnick, S.: Hyperproteinemia: Its Significance, Internat. Clin. **3**:248-279 (Sept.) 1937.

the ninth postoperative day, when there developed chills and fever daily associated with leukopenia. Malarial parasites were observed in large numbers in the blood smear. After six days of quinine therapy the reaction to the first Kahn test of the blood was reported strongly positive. The total protein content of the serum was 8.8 Gm. per hundred cubic centimeters, the albumin 4.2 Gm. and the globulin 4.6 Gm. A careful study of the patient, his wife and newborn infant failed to reveal any evidence of syphilis. Table 2 presents the pertinent data and reveals spontaneous regressions of the serologic reactions as the total protein and serum globulin tend to return to normal with improvement in the patient's condition, although no antisyphilitic treatment had been administered.

Pregnancy has long been assumed to be associated with a false positive reaction. This would seem to be exceptional from our stand-

TABLE 2.—*Laboratory Data of a Patient with Malaria and Biologic False Positive Serologic Reactions for Syphilis*

	Serologic Reactions			Protein, Gm. per 100 Cc.		
Date	Kolmer	Kahn	Kline	Total	Albumin	Globulin
9/26/41	Negative – – (Qualitative)	444	+++			
10/3/41	Doubtful Positive 1 – – – – (Quantitative)	344	+	8.8	4.2	4.6
10/10/41	Negative	111	+	7.6	3.9	3.7
10/30/41	Negative	Negative	..	6.7	5.1	1.6

point, since it is known that during pregnancy the total blood protein is somewhat reduced rather than elevated. However, Plass and Matthew [6] stated that in spite of the reduction in the total protein the euglobin and fibrinogen fractions are increased. Furthermore, since the Kahn flocculation test has displaced the complement fixation test routinely, false positive reactions in pregnant women are rare.

We have observed 34 cases of hyperproteinemia associated with a variety of conditions.[7] Most of these cases were detected by making total protein determinations by the Kagan falling drop method [8] routinely on large numbers of blood serums submitted to the laboratory of the Cook County Hospital for serologic examination. In 8 of these

6. Plass, E. D., and Matthew, C. W.: Plasma Protein Fractions in Normal Pregnancy, Labor and Puerperium, Am. J. Obst. & Gynec. **12**:346-358 (Sept.) 1926.

7. Cardon, L.; Atlas, D. H., and others: To be published.

8. Kagan, B. M.: A Simple Method for the Estimation of Total Protein Content of Plasma and Serum: II. The Estimation of Total Protein Content of Human Plasma and Serum by the Use of the Falling Drop Method, J. Clin. Investigation **17**:373-376 (July) 1938.

TABLE 3.—*Patients with Hyperproteinemia and Hyperglobulinemia with False Positive Serologic Reactions*

Patient	Protein,* Gm. per 100 Cc.			A/G Ratio	Formol-Gel [9] Reaction	Takata-Ara [10] Reaction	Sedimentation Rate †		Serologic Reactions		Diagnosis
	Total	Albumin	Globulin				Uncorrected	Corrected	Kahn	Wassermann	
M. D.‡	10.15	3.61	6.54	0.55	++++	++++	120	80	+++	Anticomp.	Chronic pyelonephritis
	8.42								+	Neg.	
A. B.‡	8.78	2.05	6.73	0.30	++++	++++	125	87	++	Anticomp.	Cirrhosis of the liver and alcoholism
									Neg.		
C.N.§	9.38	2.87	6.51	0.42	..	..	...	..	++++	Neg.	Cirrhosis of the liver and alcoholism
E. H.	8.87	....	....	....	..	..	100	52	+++	Neg.	Otitis media and erysipelas
	7.35								Neg.		
A. J.	10.5	....	....	....	..	..	95	92	+++	Neg.	Acute pyelonephritis and dehydration
	8.04	....	....	....	++++	++++					
E. B.	9.56	....	....	....	..	..	...	..	+++	Neg.	Chronic alcoholism with deterioration
H. W.	8.49	....	....	....	++	Neg.	70	..	++++	- -	Myelitis, paraplegia and dehydration
	7.08	....	....	....	Neg.	Neg.			++++	Neg.	
									+	Neg.	
D. W.	8.23	4.35	3.88	....	++	++	110	90	+++	Neg.	Pneumonia

* Total protein was obtained by the Kagan falling drop method [8]; the other values were obtained by the micro-Kjeldahl method.

† Sedimentation rates were obtained by the use of Westergren tubes on oxalated plasma and corrected for red cell volume (hematocrit) according to Plass and Rourke (Plass, E. D., and Rourke, M. D.: A New Procedure for Determining Blood Sedimentation Rate, J. Clin. Investigation **5**: 531-539 [June] 1928). Values for uncorrected sedimentation rates are given in millimeters per hour.

‡ Frei tests gave negative results.

§ Diagnosis established by postmortem examination.

cases (23 per cent) what we considered to be biologic false positive reactions were obtained (table 3). It can be seen from the table that it is the flocculation test and not the complement fixation test that is most likely to give the false positive reactions with hyperproteinemia.

The verification tests were not performed in our cases, since our work was not primarily directed toward the false positive reaction, and the correlation here presented was accidentally detected in analyzing our data on hyperproteinemia. The interpretation of the positive serologic reactions in our cases as being of the biologic false type is, from the very nature of the problem, more or less arbitrary, but it is supported by the following considerations, some presumptive and others more significant: (1) absence of clinical evidence of syphilis (autopsy performed in 1 case [C. N.] revealed no evidence of syphilis); (2) reversal of a weakly positive reaction to negative or of a strongly positive reaction to a weak one during a short period of observation, without antisyphilitic therapy; (3) association of a strongly positive Kahn reaction with a negative Wassermann reaction in the absence of history or signs of early syphilis; (4) presence of an anticomplementary Wassermann reaction. We were influenced also by the correlation we had noted in the literature, as presented in table 1.

In only 1 other case in our series of 34 was there a positive serologic reaction of the blood. In this case both the Kahn and the Wassermann reaction were strongly positive, and this patient was considered to be syphilitic. Thus, in 8 out of 9 cases in which positive serologic reactions were obtained in this series of 34 cases of hyperproteinemia the reaction was considered to be of the biologic false positive type.

It is generally known that the reactions to formol-gel [9] and Takata-Ara [10] tests are largely dependent on an increase in the globulin fraction,[5] and, as it is almost always the globulin that is increased in hyperproteinemia, these tests have frequently been used as a simple means of detecting or confirming the presence of hyperproteinemia. They are, however, not sensitive enough to detect slight to moderate increases in the globulin content of the blood.

It is important in this connection to know the behavior of the total serum protein and globulin values in patients with uncomplicated syphilis. The earlier investigators in this field reported that moderate elevations in the total serum protein and globulin fractions were commonly found in the active stages of the disease.[11] However, the more recent reports on large series of cases of syphilis indicate that little

9. Kirk, R. C.: The Takata-Ara Test and Its Relation to Cirrhosis of Liver, J. A. M. A. **107**:1354-1357 (Oct. 24) 1936.

10. Ragins, A. B.: Value of the Takata and Ara Reaction as a Diagnostic and Prognostic Aid in Cirrhosis of Liver, J. Lab. & Clin. Med. **20**:902-913 (June) 1935.

11. Lloyd, R. B.: Protein Graphs in Syphilis with Their Relation to the Wassermann Reaction, Indian J. M. Research **19**:1055-1075 (April) 1932.

if any alteration in the concentration of plasma proteins occurs in uncomplicated cases and that the elevations previously reported were probably due to complicating conditions, especially lymphogranuloma venereum. The latter fact was clearly demonstrated by Jones and Rome.[12] In a small series of cases we have confirmed this.[7]

The association of the false positive reaction and hyperglobulinemia if substantiated may explain the elevation of the sedimentation rate in some of the cases with false reactions in a different manner than that implied by Moore. Specifically, the elevated sedimentation rate may be directly related to the alterations in blood protein, as indicated previously in this report.

Our results seem to indicate that in most cases of hyperproteinemia this condition is not associated with false positive reactions. This statement cannot be made without reservation, however, since the false positive serologic reaction may occur as a transient phenomenon during the course of even a persistent hyperproteinemia. This is illustrated by the case of H. P. (a private patient of one of us [L. C.], reported elsewhere,[7] and not included in the table), in which at one time early in the course of a bacterial endocarditis a 2 plus Kahn reaction and a negative Wassermann reaction were obtained. Throughout the subsequent course, over a period of eighteen months, during which repeated high values of the total serum protein and globulin and two anticomplementary Wassermann reactions were obtained, the Kahn reaction of the blood remained persistently negative. Had the patient not been under observation at the time the false positive reaction was present, the case would have been wrongly classified as one of hyperproteinemia without a false positive reaction. It is possible, then, that the false positive reaction may occur in hyperproteinemia with much greater frequency than our table would indicate.

We realize that our small series of cases of biologic false positive serologic reactions associated with hyperproteinemia is far too small to enable us to draw definite conclusions. Nevertheless we feel that the material presented here gives some ground for the belief that there may be some relation between the biologic false positive reaction to the serologic test for syphilis and hyperglobulinemia. We suggest, therefore, that in addition to the procedures outlined by Moore, Eagle and Mohr for detecting the false positive reaction, the total protein and serum globulin concentrations be determined in cases in which such a reaction is suspected.[13] If either of these two values or both are

12. Jones, C. A., and Rome, H. P.: Serum Proteins, Takata-Ara Reaction, and Liver Function Tests in Lymphogranuloma Venereum, Am. J. Clin. Path. 9:421-436 (July) 1939.

13. When large numbers of determinations must be made (as in selective service examinations) the falling drop method for determination of total serum

(Footnote continued on next page)

increased or (and) if the Wassermann reaction is anticomplementary, then the probability of a false positive reaction is great and procedures should be instituted to rule out the conditions which are known to cause hyperproteinemia and hyperglobulinemia. For apparently normal persons the Frei test for lymphogranuloma venereum is especially important. Further investigations along these lines are indicated.

SUMMARY AND CONCLUSIONS

Attention is called to the similarity between conditions that may give biologic false positive serologic reactions or anticomplementary reactions to complement fixation tests and the conditions that may be associated with hyperproteinemia and hyperglobulinemia.

Biologic false positive reactions were observed in 8 of 34 cases (23 per cent) of hyperproteinemia (and in 2 cases independent of this series) associated with a variety of conditions. It is suggested that the incidence may be even greater than these figures would indicate. This is compared with the normal incidence of 1 false positive reaction in every 4,000 normal persons.

In 8 of the total of 9 cases in this series in which the serologic reactions were positive the reactions were considered to be of the biologic false type.

The Kahn and Klein flocculation tests more frequently gave false positive reactions than the complement fixation tests.

It is suggested that blood protein studies be instituted when a false positive reaction is suspected; increase in either the total serum protein or the serum globulin or in both or the presence of an associated anticomplementary Wassermann reaction is strongly suggestive of a biologic false positive serologic reaction.

Care should be taken in the interpretation of a positive serologic reaction for syphilis in the presence of conditions associated with hyperproteinemia and hyperglobulinemia.

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protein (Kagan.[8] Barbour, H. G., and Hamilton, W. F.: The Falling Drop Method for Determining Specific Gravity, J. Biol. Chem. **69**:625-640 [Aug.] 1926) is simple, rapid, accurate and relatively inexpensive. The formol-gel test is a comparatively simple procedure which can be used to demonstrate hyperglobulinemia if this is moderate or marked but cannot be depended on with certainty for mild elevations, which may nevertheless be of clinical significance. The chemical determination would then have to be carried out.

RAGWEED DERMATITIS AMONG WORKERS IN THE FLOUR AND GRAIN INDUSTRIES

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Eczematous dermatitis due to sensitization to the common ragweed plant (Ambrosia artemisiaefolia) has frequently been observed in farmers and others engaged in work in the open fields. The dermatitis in workers of this type usually appears in August, during the period when ragweed pollenates, and disappears soon after the first frost. Persistence of the dermatitis beyond the appearance of frost may be due to the presence of the oleoresins, particles of the weed or pollen in the clothing or to the presence of particles of the weed or pollen in dust about the barn or elsewhere. Ragweed sensitization is frequently accompanied by sensitization to pyrethrum, turpentine, burweed and marsh elder (Brunsting and Anderson [1]) and in our experience also feverfew, bitterweed and in a few instances flax and its products, such as linseed oil. Thus it is possible for ragweed dermatitis to persist as a result of exposure to these plants or their products, such as paints or insecticides. The dermatitis described in this group of workers is usually of a confluent, erythematosquamous type which involves the exposed areas of the skin, principally the face, neck, forearms, cubital areas and ankles. Involvement of the penis and scrotum sometimes occurs, and in rare instances the eruption may be universal. Brown, Milford and Coca [2] established the fact that the dermatitis was due to a fat-soluble portion of the plant or pollen oil, while the protein fraction of the plant was responsible for hay fever and asthma.

Ragweed dermatitis among workers in the flour and cattle feed industries or in other industries which expose the worker to grain and grain dust has received scant attention in the literature. We have

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1. Brunsting, L. A., and Anderson, C. R.: Ragweed Dermatitis: Report Based on Eighteen Cases, J. A. M. A. **103**:1285-1290 (Oct. 27) 1934.

2. Brown, A.; Milford, E. L., and Coca, A. F.: Studies in Contact Dermatitis: Nature and Etiology of Pollen Dermatitis, J. Allergy **2**:301-309 (July) 1931.

found only one casual reference to a case (Wittich [3]). It is our opinion that sensitization to ragweed oil is common among workers in these industries and is a frequent cause of severe occupational dermatitis. We therefore wish to report the following 9 cases and discuss ragweed dermatitis in these industries.

REPORT OF CASES

CASE 1.—R. S., a white man aged 60, first presented himself on June 30, 1936 with a confluent erythematosquamous dermatitis about the face and neck, in the cubital areas, on the forearms and in patchy areas about the ankles. The eruption had been present six months. He had been employed as an electrician in the grain elevator for several years, and during the course of his work grain dust precipitated on his skin. Patch tests were performed with common weeds, dust from the grain elevator and a fresh leaf from a ragweed plant. The reactions to tests with the ragweed leaf and the dust from the mill were strongly positive. Attempts were made to desensitize the patient by subcutaneous injections of the oil derived from the ragweed plant, without success. During the course of the next year he had repeated exacerbations of the dermatitis each time he was exposed to the dust of the grain elevator, and subsequently he had to discontinue working in the grain elevator because of the dermatitis. Since discontinuing this type of work he has remained free of the eruption.

CASE 2.—A. N., a white man aged 41, was first seen on June 6, 1939 with a confluent erythematosquamous dermatitis involving the face, neck, cubital areas and lower part of the abdomen. The eruption had been present for three weeks. He had been employed as a worker in a cattle feed mill for several years, and for some time before the dermatitis developed he had been transporting bags loaded with mash feed to railroad cars. Patch tests were performed with the mash feed, dust from the mill and a 10 per cent alcoholic solution of oil derived from ragweed pollen. The reactions to all the tests were strongly positive. He was advised to discontinue work, and the dermatitis disappeared completely in five weeks. He returned to work and in two days had a recurrence of the eruption. He was therefore instructed to change his occupation to avoid further exposure to the dust.

CASE 3.—O. H., a white man aged 40, was first seen on June 7, 1939 with a confluent erythematosquamous dermatitis of the face, neck and arms and with scattered papular lesions on the trunk. The eruption had been present for one month. He had been working for several years in the mill, engaged in the manufacture of dairy feed. Patch tests were made with several samples of feeds, mill dust and a 10 per cent alcoholic solution of ragweed oil. He had a strongly positive reaction to one of the feeds and to the ragweed oil. He was told to discontinue work, and the eruption disappeared in approximately three weeks. He then went back to his original work, and the dermatitis reappeared in two or three days. Work was again discontinued until the dermatitis disappeared. His employment was then changed to office work at the mill, where there was a minimum of dust, but in spite of this the dermatitis reappeared. He was therefore advised to discontinue work at the mill entirely and has been free of the eruption except for one occasion, when he went hunting in October through fields where ragweed was growing.

3. Wittich, F. W.: Nature of Various Mill Dust Allergens, Journal-Lancet **60**:418-421 (Sept.) 1940.

CASE 4.—C. K., a white woman aged 24, was first seen on Oct. 19, 1939. At this time she had a confluent erythematosquamous dermatitis of the face, neck and cubital areas. The eruption had been present for two months. She had been working for a year in a mill where cattle feed was manufactured. She sorted cloth bags in which grains had been stored. Patch tests were performed with samples of dust, cattle feed and the ragweed oil. The reactions to the tests were strongly positive. She was instructed to discontinue work, and the eruption disappeared in three weeks. She then returned to work sorting new bags in which no grain had been stored, and thus far she has had no recurrence of the dermatitis.

CASE 5.—A. B., a white man aged 29, was first seen on Feb. 10, 1940 with a confluent erythematosquamous dermatitis on the lower part of the abdomen and upper part of the thighs. The eruption had been present for one week. He had been working in a feed mill for several months, and during the course of his occupation he transported bags of cattle feed. These he supported against his abdomen and thighs. Patch tests were made with a sample of the feed and with ragweed oil. He had a papular reaction to both substances. He was instructed to continue work and wear impervious rubber aprons. He has not been seen since.

CASE 6.—F. W., a white woman aged 31, was first seen on June 11, 1940 with an erythematosquamous dermatitis involving the cubital areas and with a history of having had a similar dermatitis on the face five weeks previously. The eruption in the cubital areas had been present two weeks. She had been employed for several months in a feed mill, and her principal occupation was cleaning bags in which grain had previously been stored. Patch tests were made with ten different dusts and feeds and with ragweed oil. She had a strongly positive reaction to one of the feeds and a vesicular reaction to the ragweed oil. The eruption disappeared entirely when she was away from work for two weeks.

CASE 7.—G. L., a white man aged 31, was first seen on July 25, 1940 with a confluent erythematosquamous dermatitis on the face and neck and to a lesser extent on the legs and thighs. The eruption had been present about one week. He had worked in a feed mill for the past year loading bags with cattle feed. Patch tests were performed with dust from the mill and with ragweed oil. Both substances produced a vesicular reaction. He was told to discontinue work, and the eruption cleared up entirely in the course of three weeks. He returned to work at the mill on a job where there was less contact with the dust but continued to have mild periodic outbreaks during the course of the next six months whenever there was slight contact with grain dust. He was finally advised to discontinue work at the feed mill. When he was seen three months later there had been no recurrence of the eruption.

CASE 8.—M. M., a white man aged 45, was first seen on Oct. 5, 1940 with a confluent erythematosquamous dermatitis involving the face, neck, cubital areas and right leg. He worked for several years in a flour mill, where he was exposed to grain dust. Patch tests were performed with several samples of flour, soap, dust from the mill and ragweed oil. The test with ragweed oil elicited a strongly positive reaction, and tests with the other substances, negative reactions. He was advised to protect his skin more fully from dust by wearing additional clothes and covering as much as possible the exposed areas. The eruption slowly improved. He was last seen on November 12, and his skin was free of eruption.

CASE 9.—F. H., a white man aged 43, was first seen on April 28, 1942, when he presented himself with a confluent erythematosquamous dermatitis on the dorsal surfaces of the hands and wrists and about the neck. The present attack was of

two weeks' duration, but he had had similar attacks of greater or lesser severity for fifteen years. He was employed as a rigger on Great Lakes boats, many of which carry grain or flax products. He had noted that he was particularly liable to have the eruption when working on a grain boat. Patch tests were made with all common weeds, including ragweed and flax products. He had strongly positive reactions to short ragweed, feverfew, march elder and linseed oil, as well as to flax seed itself.

COMMENT

Dermatitis due to ragweed, similar to that reported among farmers and others exposed to the growing plant, is also an industrial hazard among workers in the flour and grain industries. The eruption is essentially the same in both types of workers. It is usually erythemato-squamous and confluent and in most instances confined to the exposed areas of the skin.

The seasonal incidence which is so striking among the first group exposed to the growing plant is different among grain workers. The eruption may appear any time during the year but is most apt to appear or increase in severity during the warm months, when perspiration causes dust particles to adhere to the skin. The diagnosis of ragweed dermatitis should be suspected in cases of dermatitis venenata among grain workers, and patch tests with ragweed oil, extracts or a leaf from the plant should be performed. In our experience patch tests have been highly diagnostic in this group. Most workers in the flour and grain industries who have a dermatitis from ragweed eventually find it necessary to undergo a total change of employment. They should be instructed to avoid insect sprays containing pyrethrum. They should be warned against exposure to marsh elder, burweed, feverfew and bitterweed, as well as the growing ragweed plant, and to prevent exposure to pollen as much as possible during the period of pollenization by avoiding proximity to open fields.

SUMMARY

1. Case histories of 9 patients employed in the flour and grain industries who had a dermatitis due to ragweed are presented.

2. Ragweed dermatitis is a common industrial hazard among this group of workers.

3. The dermatitis observed in this group of workers is similar to that seen in farmers or others engaged in work in the open fields.

4. Patch tests made with alcoholic extract of the weed, pollen oil or a fresh leaf from the plant are highly diagnostic.

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CISTERNAL PUNCTURE

A FAVORABLE REPORT BASED ON OVER SIX THOUSAND PUNCTURES

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AND

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For ten years puncture of the cisterna magna has been a routine procedure with us in our clinic work, as well as in our private practice. In this period 6,123 punctures have been made, and we have yet to encounter a serious reaction or even a reaction severe enough to require rest in bed for a single patient.

Moore [1] and a group of other workers are distinctly opposed to the use of cisternal puncture for routine diagnostic purposes. There is no doubt but that the opponents of its use base their opinions on sound reasons. We believe, however, that their convictions are not completely justified. We feel that in the proper hands cisternal puncture can occupy a place as prominent as that of lumbar puncture.

Success with this procedure, as well as with all other technical procedures, is dependent on experience, clinical judgment and the natural technical ability of the operator. The opponents of this method as a routine procedure feel that cisternal puncture should be reserved for special instances,[2] such as therapeutic injections, and as a diagnostic aid. But how can one develop a technic that is fine enough to compensate for the additional risk involved in such cases unless one has experience with the method? Only vague impressions can be formed from reading textbooks or articles. Enough skill cannot be gained on the cadaver.[3] Experience and skill can be gained (with the proper teaching, guidance and supervision) only by performing a large number of punctures in patients.

From the Dallas Syphilis and Venereal Disease Clinic, Department of Health, Parkland Hospital.

1. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1941, p. 179.

2. (*a*) Merritt, H. H., and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Company, 1938, p. 84. (*b*) Moore.[1]

3. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1934, p. 408.

The technic [4] of cisternal puncture is given in detail in several textbooks and published articles and therefore is omitted in this paper. We feel, however, that we should emphasize several points. The contraindications for cisternal puncture are the same as those for lumbar puncture. We strongly recommend the prone position. Placing the patient in the proper position is important. A beginner should remove the stylet before entering the cisterna magna. This is not necessary in the hands of the more skillful operator, but all should proceed cautiously. Sometimes it is necessary to start the flow of fluid with a syringe.

We do not wish to minimize the actual risks that exist. It cannot be denied that there are anatomic risks. One must remember also the possibility of the presence of anomalies. Dandy's case of an anomalous artery [5] is a striking example. We fear this more than injury to the medulla oblongata. However, the danger of puncture of an anomalous artery exists also in the lumbar region.

The advantages of cisternal puncture over lumbar puncture cannot be overemphasized. If these advantages are not overshadowed by risk, then cisternal puncture has a definite place as a routine diagnostic measure in the management of syphilis. This has been our experience. In our series of over 6,000 punctures we have encountered no fatalities and no reactions which we considered serious—certainly none as serious as is often experienced following lumbar puncture.

The first demonstration [6] of cisternal puncture in this country was made in 1927 by Dr. Alois Memmesheimer, from Hoffman's clinic, and was given at the New York University College of Medicine. After this the procedure was adopted by many physicians, and, as shown by the large series of punctures performed by different operators, its merits have been proved.

Saunders [6] has made about 12,000 cisternal punctures and Spiegel [6] over 11,000. Neither of these operators had a fatility. Petersen [7] reported 4,300 punctures without a fatality, and Kulchar [8] encountered no serious accidents in more than 2,500.

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4. (*a*) Fox, E. C.: Cistern Puncture in the Diagnosis and Treatment of Syphilis, Texas State J. Med. **28**:534-535 (Dec.) 1932. (*b*) Moore.[1] Merritt and Fremont-Smith.[2a] Stokes.[3]

5. Dandy, W. E.: Treatment of Intracranial Hemorrhage Resulting from Cisternal Puncture, Bull. Johns Hopkins Hosp. **56**:294-301 (May) 1935.

6. Fox, H.: Personal communication to the author.

7. Petersen, M. C.: Cisternal Puncture with Special Reference tc the Aged, J. A. M. A. **110**:953 (March 26) 1938.

8. Kulchar, G. V.: Cisternal Puncture: A Survey of the Reactions Following 1,246 Punctures, Am. J. Syph., Gonor. & Ven. Dis. **24**:643-650 (Sept.) 1940.

Reactions which are severe enough to cause patients to seek medical care for relief may be considered as serious. One might also consider as serious those reactions of which the patients volunteer complaints on their return visits. These occurrences are not rare [9] following lumbar puncture, ranging from 25 to 50 per cent in ambulatory patients.

In our experience, reactions following cisternal puncture have been of a mild character. Few of our patients had headaches which were severe enough to cause them to complain, and no headaches were severe enough to require rest in bed. It has been rare for our patients to have any complaint other than slight tenderness or stiffness at the site of the needle puncture. All of our patients have been ambulatory.

To stresss further the low incidence of reactions from cisternal puncture and the relative safety of the procedure, Fox [4a] reported that as many as 50 punctures were performed on a single patient. Many patients who have had both lumbar and cisternal punctures say they prefer the latter procedure. Many of our patients have had 2 and 3 punctures, and several have had 4 and 5. Our experience is in accord with that of Kulchar [8] and Davenport,[10] who found a lower incidence of reactions and reactions of less severity after cisternal than after lumbar puncture.

SUMMARY AND CONCLUSIONS

During a period of ten years we have made 6,123 cisternal punctures. There has not been any reaction of serious consequence.

We feel that cisternal puncture is a valuable procedure in the proper hands and should be used more widely in syphilotherapy. We do not agree with those who consider the procedure too dangerous for routine use.

The economic importance of this procedure is obvious, since patients do not require rest in bed after the puncture.

1719 Pacific Avenue.

9. (*a*) Kulchar, G. V., and King, A.: Use of Sodium Amytal in Prevention of Reactions Associated with Lumbar Puncture, Arch. Neurol. & Psychiat. **30**:170-174 (July) 1933. (*b*) Footnotes 4, 5, 6, 7 and 8.

10. Davenport, K. M.: Postpuncture Reactions: A Clinical Study, New York State J. Med. **39**:1185-1187 (June 15) 1939.

USE OF VITAMIN A IN KERATOSIS BLENNORRHAGICA

SUCCESSFUL TREATMENT WITH MASSIVE DOSES: REPORT OF A CASE

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It is known that vitamin A is a physiologic prophylactic against infection by virtue of the fact that it guards the barrier of integrity of the epithelial linings of the mucous membranes and the skin. The high incidence of infection in experimental animals deficient in vitamin A is the usual and early observation of all research workers.[1] Accumulating experimental evidence tends to support the hypothesis that vitamin A also plays a part as an anti-infectious agent. Bloch,[2] noting many severe infections in his original studies on vitamin A deficiency in infants, maintained that vitamin A is of special importance to the organism for resisting and overcoming infection.

The histologic changes in cases of A avitaminosis have been studied by several investigators. Wolbach and Howe [3] concluded that the outstanding change is a substitution of stratified keratinizing epithelium for normal epithelium in various parts of the respiratory tract, eyes and genitourinary tract. This histologic change characterized by a transformation of cuboidal into keratinized cells is directly due to the nutritional deficiency; infection then readily attacks the weakened tissue. According to Tyson and Smith,[4] the principal changes associated with vitamin A deficiency in rats are metaplasia of cuboidal or columnar epithelium in certain parts of the body, epithelial hyperplasia in various structures and infection.

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1. Eusterman, G. B., and Wilbur, D. L.: Clinical Features of Vitamin A Deficiency, J. A. M. A. **98**:2054 (June 11) 1932.

2. Bloch, C. E.: Effects of Deficiency in Vitamins in Infancy, Am. J. Dis. Child. **42**:263-278 (Aug.) 1931.

3. Wolbach, S. B., and Howe, P. R.: Tissue Changes Following Deprivation of Fat—Soluble A Vitamin, J. Exper. Med. **42**:753-777 (Dec.) 1925.

4. Tyson, M. D., and Smith, A. H.: Tissue Changes Associated with Vitamin A Deficiency in the Rat, Am. J. Path. **5**:57-70 (Jan.) 1929.

In gonorrhea, the infecting organism attacks primarily the genital tract. It does this by first invading the epithelial lining. This system, both male and female, is lined by a single layer of epithelium, which is readily penetrated by the gonococcus. The cornified squamous epithelium of the vulva and vagina is seldom affected except in children, in whom it is soft and delicate. Once infection is established it is resistant to treatment. Recently the administration of estrogens has materially shortened the course of this disease by converting this delicate epithelium into the more resistant adult form. Yet any one with practical experience in this disease has noted the discrepancy between the laboratory findings and the clinical evidence of the disease. When routine vaginal smears are made in an institution, gram-negative intracellular diplococci are not infrequently found in children who show no symptoms of any kind. It is possible that in many of these children the organism is not the gonococcus but Micrococcus catarrhalis, which is morphologically indistinguishable from the gonococcus and also capable of causing vaginitis in children. Yet it is also possible that the organism is the gonococcus and that these children possess sufficient vitamin A to preserve the physiologic integrity of the epithelial surface. This line of thought may even be extended to include the other less frequent complications of gonorrhea, namely, keratosis blennorrhagica, conjunctivitis, arthritis and endocarditis. Do these lesions develop in patients who do not have an adequate supply of vitamin A? Would they be prevented or cured by the ingestion of massive doses of vitamin A?

Keratosis blennorrhagica is a rare disease. It occurs almost exclusively in men during the third and fourth decades. The disease is characterized by the formation of hornlike lesions, discrete or diffuse, affecting special areas and occurring during the course of an attack of gonorrheal urethritis.[5] Chills and fever of a septic type herald the appearance of each crop of new lesions. The distribution of the eruption is symmetric. There is a predilection for the soles, palms, genitals and groins. Less often the scalp, dorsa of the hands and feet, forearms and legs are involved. The lesions occur usually as isolated, but sometimes confluent, hornlike crusts. The smaller ones may be semitransparent and waxy; the larger are brownish. At times vesicles precede the hornlike lesions. On the palms and soles diffuse thickening occurs, with nodular elevations, the appearance of which has been likened to that of mountain ranges on a relief map.

The cutaneous lesions are usually preceded by involvement of the joints. This arthropathy differs from the usual gonorrheal monoarthritis in the simultaneous involvement of a large number of joints. The pains are excruciating, but not as much redness and periarticular edema are present as in rheumatoid arthritis or monoarthritic gonorrheal arthritis.

5. Combes, F. C.; Dietrich, C., and Cohen, J. A.: Keratosis Blennorrhagica, J. A. M. A. **114**:2078 (May 25) 1940.

The histologic change is principally parakeratosis. The fundamental changes are epidermal vesiculation with intracellular and intercellular edema. There is a subsequent leukocytic reaction followed by pustulation and rapid formation of a dry parakeratotic scale surmounted by a crust. The crust is often a prominent feature.

The genesis of keratosis blennorrhagica is as yet unsettled. The consensus is that it is an allergic expression of a sensitized skin, similar to the conception of the tuberculid reaction. The lesions have also been interpreted as a manifestation of gonococcic septicemia in the presence of a severe arthropathy, although the finding of the gonococcus in the lesions has been extremely infrequent.

The ultimate fate of patients affected with this syndrome is variable. Local treatment is of little value. Autogenous and stock vaccines are of no value. Infusions of saline and dextrose solutions and a high caloric diet are helpful. Sulfanilamide and derivatives of it and arsphenamine have been administered, with inconsistent results. The induction of artificial fever by various means has been of value. Intravenous injections of typhoid-paratyphoid vaccine have not been attended by consistent results. Fever therapy by means of the inductotherm is sometimes of considerable value. However, as in this case, it may be followed by a relapse after a certain period and then prove of no value in treatment. In addition, the induction of a high temperature over an extended period is not without danger in debilitated or aged persons.

The use of massive doses of vitamin A in the treatment of keratosis blennorrhagica was suggested as a result of the preceding observations as well as by the beneficial effects observed in keratosis pilaris and keratosis follicularis following its use in large amounts. The similarity, both clinically and histologically, of the lesions in these otherwise unrelated diseases to the lesions of keratosis blennorrhagica lent additional support to the suggestion. The unusual rapidity of response in this extremely recalcitrant and uncommon disease is worthy of report.

REPORT OF CASE

C. G., a Negro aged 41, was admitted to Bellevue Hospital in January 1939. He had had several attacks of gonorrheal urethritis during the preceding three years. He was an alcoholic addict. About the end of November some pain developed in the left ankle with associated redness and edema. Within a few days the left knee, right ankle, right knee and left shoulder were similarly affected, in that order.

On admission he was moribund. His weight had decreased from 160 to 105 pounds (from 73 to 48 Kg.). There was extreme wasting of the muscles, especially those of the thighs and legs. He suffered excruciating pains in both upper and lower extremities, with complete loss of active motion. All large joints of both extremities were red, swollen and tender. There were moderate limitation of motion, slight swelling and tenderness of the left shoulder joint. Both seminal vesicles were tender and distended, and the prostate was enlarged and boggy.

The cutaneous lesions were generalized but more profuse on the lower extremities. There were two distinct varieties, keratotic papules and irregularly shaped, well defined plaques. The former were confined to his hands and feet. Some of them were situated beneath the free border of the nails, which were in some instances elevated from the nail bed and distorted. Irregularly distributed over the back of his feet, hands, legs, forearms, genitals, groins and abdomen were well defined keratotic plaques varying from 3 to 10 cm. in diameter. These were roughly conical and composed of laminated brownish yellow scales, with a hard, irregular surface.

The frontal region of the scalp was more or less covered by a scale, the layers of which were cemented together by a dried serosanguinous secretion. This extended beyond the margin of the hair onto the forehead. It was firmly adherent to the underlying skin and on removal left a smooth, superficial, dusky red, dry, eroded surface.

The patient's legs and feet at the beginning of treatment, September 1941.

Smears of material from the urethra were positive for gonococci. Examination of the blood on admission revealed erythrocytes 3,800,000, hemoglobin 75 per cent and leukocytes 7,600, with a differential ratio of polymorphonuclear leukocytes 64 per cent, lymphocytes 32 per cent and mononuclear leukocytes 4 per cent. The antifibrinolysin time was seven minutes; the hemolytic streptococcus agglutination test gave negative results, and the hemolytic streptococcus precipitin reaction (C) was plus-minus. The coagulation time was four minutes, bleeding time seven minutes, Wassermann reaction of the blood negative, reaction to gonococcus fixation test negative and blood culture (ascitic fluid) negative. The chemical examination of the blood showed chlorides 429 mg., sugar 89 mg. and nonprotein nitrogen 32 mg. per hundred cubic centimeters; the icterus index was 4 and the van den Bergh reaction negative.

For one week after admission sulfanilamide was administered in doses of 1 Gm. four times daily. In consideration of his profound prostration the patient was given pills of ferrous carbonate, viosterol in oil, thiamine hydrochloride, riboflavin and nicotinic acid, 0.1 Gm. five times daily. In addition he received liver extract

intramuscularly every other day and five blood transfusions. With this treatment he rallied and showed considerable clinical improvement, although the erythrocyte count fell to 2,900,000 and the hemoglobin level to 50 per cent. The administration of sulfanilamide had been discontinued, but because of a recurrence of pain it was resumed, with little benefit.

Beginning on March 3 and continuing at forty-eight hour intervals he received eleven treatments with the inductotherm. At each session his temperature was maintained at 104 F. for from three to four hours. The cutaneous lesions and the arthritis subsided sufficiently to permit his discharge from the hospital.

The patient remained well until July 1941. At this time he experienced a recurrence of pain in his joints. The elbows, knees, fingers and hips became tender and swollen. At the same time there appeared a cutaneous eruption similar in nature and distribution to the one present in 1939. Within two months the joints became so painful that the patient was unable to move without suffering excruciating agony. He was unable to open his mouth more than 1 inch (2.5 cm.) because of pain in the temporomandibular joints.

He was readmitted to Bellevue Hospital on September 16 and immediately given a high vitamin, high caloric diet and sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) in doses of 2 Gm. three times daily. On the second day, the dose was modified to 1 Gm. every four hours. After eleven days, administration of the drug was discontinued because of lack of improvement. The patient then received three treatments with the inductotherm. At each session his temperature was maintained at 106 F. for five hours. After the third, the patient became nauseous and vomited blood-streaked material. The fever treatments were discontinued until October 15. On this date, the fourth session provoked a similar response, and, in addition, the patient became psychotic for several hours. At this time, new cutaneous lesions appeared on the extremities in the form of pinhead-sized to pea-sized keratotic papules. They were so numerous that they practically covered the arms and legs. A smear of material from these cutaneous lesions showed gram-negative diplococci morphologically typical of Neisseria gonorrhoeae. Sulfathiazole was again administered, in doses of 1 Gm. every four hours, supplemented by 5 Gm. of sodium sulfapyridine (sodium salt of 2-[paraaminobenzenesulfonamido]-pyridine) intravenously every day in order to maintain a blood level of 2 to 3.3 mg. per hundred cubic centimeters. The patient's condition became steadily worse. His temperature began to fluctuate between 100 and 103 F. The joints remained painful, and the cutaneous lesions became more extensive despite the use of 5 per cent sulfathiazole ointment locally. Chemotherapy was discontinued on November 7, after a three week trial period. The patient had been maintained during this time on a high caloric, high vitamin diet. He had also received several small doses of gonococcus filtrate. On November 12 the daily diet was supplemented by the addition of a fish liver oil containing 200,000 U. S. P. units of vitamin A per gram. Within two weeks, there was a spectacular change in the cutaneous eruption. Many of the lesions had disappeared, and others were considerably flattened. The arthritic symptoms were sufficiently abated to permit active motion. By December 3 the patient was walking around the ward. The keratoses rapidly disappeared, and the patient left the hospital on December 19.

COMMENT

A study of the functions and properties of vitamin A and the results of massive dose therapy in this case led us toward certain conclusions. Perhaps keratosis blennorrhagica appears only in those patients with

gonorrhea who have, in addition, a deficiency in circulating vitamin A, an inability to absorb vitamin A from the intestinal tract or an inability to convert provitamin A. Still another possibility is the greater need for vitamin A by certain infected persons.

Mendel [6] stated that existing knowledge permits little more than vague speculation respecting the mode of action of vitamin A. The description of the dire consequences of a deprivation of this food essential gives little insight into precisely how it functions in the tissues. One may ask whether it is a necessary integral part of structures like the epithelial cells or whether it acts as a catalyst or "regulator" of certain cellular functions. There is some debate as to whether vitamin A can properly be designated as an anti-infective vitamin, as has been done. It is likely that the vitamin helps to preserve the physiologic integrity of various epithelial structures and there to maintain the "first line of defense" against bacterial invasion. For the present it may be wiser to stress the indefinite function of the vitamin in preserving "health and vigor" rather than to herald any specific action against definite micro-organisms.

CONCLUSIONS

1. The beneficial effects of massive dose vitamin A therapy for keratosis blennorrhagica may be due to the "anti-infective" properties of the vitamin by virtue of the fact that it restores the integrity of the epithelial linings of the mucous tracts and the skin.

2. The disease may be due to a deficiency in those patients with gonorrhea who have, in addition, a deficiency in circulating vitamin A, an inability to absorb vitamin A from the intestinal tract or an inability to convert provitamin A to vitamin A or, finally, to a greater need for vitamin A by certain infected persons. Perhaps gonococcic conjunctivitis, arthritis and endocarditis would not occur as a complication of gonorrhea if the patients had an adequate or even an excess supply of vitamin A. Perhaps these complications will respond to treatment with massive doses of vitamin A. Further studies must be performed before the questions raised by this report can be answered.

104 East Fortieth Street.

2 East Fifty-Fourth Street.

6. Mendel, L. B.: Vitamin A, J. A. M. A. **98**:1981 (June 4) 1932.

FAILURE WITH CRYOTHERAPY IN THE TREATMENT OF ACNE SCARS

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WASHINGTON, PA.

The use of carbon dioxide slush as an exfoliating agent originated with Giraudeau [1] in 1925. The first report in the American literature of the use of cryotherapy in the treatment of acne was made in 1939 by Karp, Nieman and Lerner.[2] They reviewed the literature to date and reported on the treatment of 50 of their patients with acne and acne scars.

Dobes and Keil [3] reported their results in the treatment of 115 patients with acne. Only 7 with acné scars were treated in their group, and the results were unsatisfactory.

Hollander and Shelton [4] reported favorably on a series of 36 patients with acne scarring treated by cryocautery, with an average of twenty applications per patient. They judged their results by "patient reaction." Patients were questioned by an impartial member of the staff and the findings recorded statistically. They regarded cryotherapy as a method of distinct value and a worthy addition to the dermatologic armamentarium in the treatment of scarring. Dietary measures and the application of white lotion N. F. at night were used by them as supplementary treatment.

In this study I felt that it would be a fallacy to rely on memory in judging improvement. To minimize this source of error kodachrome transparencies were made at the start and at the end of the study. To supplement these a questionnaire was given to each patient to fill out. They were questioned regarding: (*a*) sensation following the treatment, (*b*) time of onset of bullae, if any, (*c*) time of onset of desqua-

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From the Department of Dermatology, University of Pittsburgh School of Medicine, Dr. William H. Guy, Director.

1. Giraudeau: Cryothérapie directe à l'aide d'un mélange de neige carbonique et d'acétone, Bull. Soc. franç. de dermat. et syph. **35**:463, 1928; La cure d'exfoliation par le mélange de neige carbonique, acétone et soufre dans l'acné, ibid. **36**: 654, 1929.

2. Karp, F. L.; Nieman, H. A., and Lerner, C.: Cryotherapy for Acne and Its Scars, Arch. Dermat. & Syph. **39**:995 (June) 1939.

3. Dobes, W. L., and Keil, H.: Treatment of Acne Vulgaris by Cryotherapy (Slush Method), Arch. Dermat. & Syph. **42**:547 (Oct.) 1940.

4. Hollander, L., and Shelton, J. M.: An Evaluation of Cryotherapy in the Treatment of Post-Acne Scars, Pennsylvania M. J. **45**:226 (Dec.) 1941.

mation, (*d*) duration of desquamation, (*e*) improvement, if any—as they felt about it and as their friends and family felt about it—and (*f*) influence of the treatment on the occurrence of new lesions. Finally, as a further basis for judging the end results these cases were observed at intervals by members of the clinic staff, Drs. W. H. Guy, F. M. Jacob, L. G. Beinhauer and others. They are in complete agreement with the opinion expressed herein.

The technical details were the same as reported by others. I used a rolling application of the tampon on which the slush was placed. I refer to rolling in contrast to gliding the sponge or tampon over the face, for by this method it was felt that the high spots of the scar would be peeled off without causing peeling of the "valleys." As soon as the sponge was removed the elevated parts were seen to be frozen white in contrast with the normal pink of the bottoms of the scars. My patients rubbed the residual sulfur from the face within five to ten minutes after termination of the treatment. No other form of therapy was employed except for patients in whom pustules developed. After I was convinced that cryotherapy had no favorable influence on the pustules I resorted to the use of 5 per cent sulfathiazole ointment in a vanishing cream base. This seemed to be of value in the treatment of the pyoderma.

The "patient reaction" in all my cases was favorable. All reported that friends and relatives commented favorably on the improvement. Probably the most convincing evidence of favorable "patient reaction" was the fact that some of my patients continued to return faithfully each week for treatment for periods ranging from one year to a year and a half. For every one who stopped treatment there was a compelling reason, such as moving out of town or getting employment that made attendance at the clinic impossible. I mention "patient reaction" in detail for the sole reason that if the study had been evaluated on this basis this paper would not be a negative report.

This report is based on a group of 20 patients treated for acne scars over a period of twenty months. A total of eight hundred and twelve treatments were given. Four patients received only eight treatments and so are not seriously considered in the final evaluation. One patient received seventy treatments; another received sixty-eight, and 3 others received over fifty treatments. This small group received more treatments per person than any thus far reported. Thirteen patients averaged thirty-seven treatments each. All of them had previously received treatment for acne. This included at least one course of sixteen unfiltered roentgen ray treatments (75 r) given at intervals to three areas of the face. In addition they had followed the usual dietary regimen for acne and had used white lotion N. F. None of these patients

could be classified as having active acne, but in all of them a few pustules or papules were appearing from time to time. One patient presented deep neurotic excoriations on an otherwise smooth skin.

SUMMARY AND CONCLUSIONS

Twenty patients were treated by cryocautery for scars that remained after routine treatment of acne. In 13 cases the average number of treatments was thirty-seven. Cryocautery offers nothing in the treatment of acne scarring that cannot be obtained with conventional, less time-consuming and less painful methods.

6 South Main Street.

VARIOLIFORM ERUPTION FROM SULFATHIAZOLE

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AND
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Various types of eruption following the use of sulfanilamide and derivatives of it are being constantly reported, but as far as we are able to learn the case to be described is the first reported instance of a varioliform eruption from sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole). Cleveland [1] described the first varioliform eruption which was thought to be due to sulfanilamide. Spink,[2] in a recent excellent monograph on the sulfanilamide compounds, stated that dermatitis is common from sulfanilamide and sulfathiazole, but he did not mention the rarer dermatoses, such as varioliform eruptions. The following case was observed by one of us (A. G. F.) at the Lawson General Hospital, Atlanta, Ga.[3]

REPORT OF A CASE

A former salesman aged 27 was admitted to the hospital on Sept. 1, 1941. He was acutely ill, with a temperature of 102 F., a pulse rate of 88 and a respiratory rate of 12. His family history was irrelevant, and his personal history was essentially normal except that he had had septicemia at the age of 20. The present eruption began suddenly with a chill but without other pain or discomfort. Physical examination showed nothing abnormal except for a moderately injected throat, a few moist rales heard over the primary bronchi and moderate tenderness over the right lumbar region, suggesting acute pyelitis and acute pharyngitis. The blood pressure was 118 systolic and 62 diastolic. A few coarse rales were heard over the primary bronchi but disappeared after the patient coughed. There was moderate tenderness over the right kidney, and pus (3 plus reaction) was found in the urine. A complete analysis of the blood showed no abnormalities except a leukocytosis (15,000 cells per cubic millimeter).

On admission the patient was given a liquid diet, fluids were forced and a 10 grain tablet of sulfathiazole was given every three hours. He continued to have a temperature of 102 F. and complained of nocturia and pain on urination with some tenderness over the right kidney. About six days after he had com-

1. Cleveland, D. E. H.: Varioliform Eruption from Sulfanilamide, Arch. Dermat. & Syph. **39**:693-695 (April) 1939.

2. Spink, W. W.: Mod. Med., November 1941, p. 53.

3. Brig. Gen. W. L. Sheep, commanding; Col. E. E. Cooley, Chief of Medical Service.

menced to take sulfathiazole tablets a moderately severe rash appeared on the neck. As it was assumed that the rash might be due to sulfathiazole, this medication was discontinued and codeine, acetylsalicylic acid and other remedies were substituted. Several days later the patient complained of mild pain in the chest and a moderate amount of thick viscid yellowish mucus was expectorated; a roentgenogram showed a small cavity in the lower lobe of the right lung and another about the size of a quarter near the hilus of the left lung. Little change occurred in the patient's condition except for slight improvement after 3,000 cc. of 10 per cent dextrose solution was given intravenously.

At this time 10 grain tablets of sulfathiazole every three hours were again administered. Two days later the administration of sulfathiazole was discontinued for the second time, because of a pustular eruption which appeared on the neck and which became progressively profuse over the entire body. The eruption was particularly severe on the neck, the arms, especially the dorsal surfaces of the axillas, the abdomen and the hips. The legs were involved to a less extent. The lesions appeared as discrete vesicles which subsequently became pustular. In some areas the eruption was at first decidedly erythematous, while in other areas there were vesicles and pustules. The entire process ran its course in seven weeks, but the individual lesions lasted only a few days. Despite the prompt discontinuance of use of the drug, apparently the formation of new crops had prolonged the duration. None of the lesions were umbilicated. No scarring was left by the eruption. There were no lesions on the mucous membranes. Treatment consisted of potassium permanganate baths and application of soothing lotions and emulsions.

A biopsy of one of the pustular lesions showed the following picture: The specimen consisted of 0.5 Gm. of cutaneous tissue, which measured 0.2 by 0.4 cm., along with subcutaneous tissue. The section revealed suppuration of the superficial layers of the corneum in some areas, while in others the exudation was more serous. There was generalized spongiosis of the epidermis and an occasional mitotic figure in the prickle cell layer. The subepithelial inflammatory reaction corresponded to the more acute areas of the exudation in the epithelium and consisted of focal and diffuse infiltrations with neutrophils, mostly perivascular, with the neutrophils almost plugging the smaller vessels. There were no plasma cells, and beneath the more active areas there was a residual edema.

The pathologist, Col. J. E. Ash, agreed that the eruption fitted into the "erythema multiforme" group and was in all probability of drug origin.

The eruption in this case resembled that described by Cleveland, even the erythema-multiforme-like lesions on which pustules were aggregated having been present.

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140 East Fifty-Fourth Street, New York.

Clinical Notes

PROPER USE OF RUBBER SPONGE DRESSINGS

THOMAS S. SAUNDERS, M.D., PORTLAND, ORE.

The rubber sponge dressing, originally suggested for the treatment of varicose ulcers, is apparently being used to treat all forms of ulceration of the leg. Such a policy must inevitably lead to therapeutic disappointments. Recently I have had occasion to observe several ulcers of the leg for which treatment with the rubber sponge had been employed initially. In all cases the history was the same: The pain and discomfort had been increased, and/or the discharge had become more profuse. Analysis of these cases showed one or two factors responsible. In some cases the sponge had been applied to a gangrenous ulcer; the pressure exerted by the sponge then tended to make the ulcer more ischemic and consequently more painful. In other cases the sponge had acted as an occlusive dressing and the resulting exudation had caused extensive maceration of the contiguous skin.

In the treatment of ulcers of the leg associated with stasis and edema the rubber sponge dressing is of great value. However, its indiscriminate use for all ulcers of the leg regardless of cause or condition, may aggravate the lesions and actually prevent healing.

Medical Arts Building.

ORIENTAL SORE POSSIBLY CONTRACTED IN THE UNITED STATES

Report of a Case

A. GELBER, M.D., LOS ANGELES

The patient is a white woman aged 53 whose occupation for the past six years has been that of a social worker in a large county hospital in southern California. Her general health has been good. She has always lived in the United States, but in 1929 she went on a six months' tour of Europe, traveling through England, France, Belgium, Austria and Italy. While skirting the Mediterranean she visited Naples and made several short inland tours.

In September 1941 she noticed a small red papule on the middle of the left cheek about the level of the zygoma. Thinking that it was a mole, she did not bother to seek medical advice. About in February 1942 she noticed that the lesion was increasing in size and thickness and was covered with crusts; when these were accidentally pulled off there would be bleeding from an underlying ulcerated area.

When first seen, the lesion was a single sharply outlined, round, soft, bulky-crusted, large pea-sized papule. It was fragile, bled readily and had a granulating floor, an edematous base with an erythematous areola about ⅛ inch (0.3 cm.) in width. The clinical appearance of the lesion was that of a granuloma, and in the differential diagnosis I considered epithelioma, syphilis and pyogenic

granuloma due to streptococcic and staphylococcic infection. There was no regional adenopathy and no pain associated with the lesion. No smears were made, but the lesion was excised by surgical diathermy and studied histologically. The resulting scar was pliable, smooth and excellent cosmetically. The peripheral blood smears were negative for Leishmania tropica.

The report of a biopsy by Drs. Satenstein and Sachs, on April 23, 1942, was as follows: "The epidermis is moderately irregularly acanthotic and verrucous. Throughout most of the upper part of the section there is a cellular infiltration composed principally of plasma cells, some small round cells and some connective tissue cells. Examination of the infiltration with the Gram stain shows the presence of leishmania bodies (Leishmania tropica)."

If the patient was infected during her trip abroad, that would constitute an incubation period of thirteen years, which would appear to be an impossibility. The most logical source of contact would be of more recent date, since in her work she comes in contact with many persons who are natives of the Near East and countries in which leishmaniasis is endemic.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

CHANCRE OF THE GUM. JOSEPH F. SADUSK JR. and BERT G. ANDERSON, Am. J. M. Sc. **203**:397 (March) 1942.

Sadusk and Anderson portray by means of color photography an instance of chancre of the gum and point out that such lesions almost always appear on the anterior portion of the upper gum, usually on the left side. They vary within wide limits of size and shape and may be either erosive or ulcerative.

DERMATITIS FROM TOPICAL APPLICATION OF 2-METHYL-1:4-NAPHTHOQUINONE (SYNTHETIC VITAMIN K ANALOGUE). R. C. PAGE and Z. BERCOVITZ, Am. J. M. Sc. **203**:566 (April) 1942.

Nine patients with chronic ulcerative colitis were treated by the application of an ointment containing synthetic vitamin K (menadione [2-methyl-1,4-naphthoquinone]). In 5 instances the skin reacted with pruritus, erythema and edema. The dermatitis was later shown to be due to the chemical and not to the specially prepared base.

LYNCH, St. Paul.

THE POLICY OF THE UNITED STATES CIVIL SERVICE COMMISSION TOWARD APPLICANTS WITH SYPHILIS. O. L. ANDERSON, Am. J. Syph., Gonor. & Ven. Dis. **26**:265 (May) 1942.

The United States Civil Service Commission is the largest employer in the United States, and perhaps in the world. The United States Public Health Service in January 1939 accepted a request by the Civil Service Commission to participate in a cooperative project with the objective of bringing the policies of the commission with respect to syphilis into line with modern scientific knowledge and experience.

The following improvements in the commission's policy toward syphilis have been made: The requirement of five years of treatment prior to appointment has been shortened. The method of evaluating eligibility for employment of persons with this malady has been brought into line with modern scientific knowledge of the disease. The policy with respect to acceptance and rejection of applicants with syphilis has been liberalized. Provision has been made for the temporary employment of persons who require further antisyphilitic treatment before they can be certified as eligible for probational appointment. In addition, the Public Health Service has recommended a confidential record system for the handling of medical certificates and reports and routine blood testing of all civil service applicants either before or after appointment. The decisions of the medical division of the Civil Service Commission with respect to physical eligibility of applicants should not be subject to the review of laymen except before judiciary or quasi-judiciary bodies.

YOLK SAC ANTIGENS IN THE DIAGNOSIS AND EPIDEMIOLOGY OF LYMPHOGRANULOMA VENEREUM. M. F. SHAFFER, G. RAKE and A. W. GRACE, Am. J. Syph., Gonor. & Ven. Dis. **26**:271 (May) 1942.

From the heavily diseased yolk sac of the developing chick embryo infected via this route with the agent of lymphogranuloma venereum, it has been possible to prepare rich suspensions of the viral elementary bodies. Such a suspension, inactivated and standardized, constitutes an antigen (lygranum) eminently suited

for use in the Frei intradermal test. Through its use it has also been possible regularly to demonstrate specific complement-fixing properties in lymphogranulomatous serums.

Both the Frei test and the complement fixation test performed with yolk sac antigen have confirmed the previous reports of high incidence of infections with the agent of lymphogranuloma venereum concomitantly with other venereal disease. Infection with the virus of lymphogranuloma venereum appears to be widespread and constitutes a serious public health problem.

THE INADEQUACY OF A SINGLE PROLONGED FEVER FOR THE TREATMENT OF EARLY ACUTE SYPHILIS. R. A. BOAK, C. M. CARPENTER, N. JONES, R. H. KAMPMEIER, W. S. MCCANN, S. L. WARREN and J. R. WILLIAMS, Am. J. Syph., Gonor. & Ven. Dis. **26**:291 (May) 1942.

A single prolonged fever treatment (ten to fifteen hours with a temperature of 41 to 41.5 C. [105.8 to 106.7 F.]) resulted in a prompt resolution of the lesions in 8 cases of primary and secondary syphilis. The lesions usually became normal on dark field examination during the single period of actual treatment. In general, the patients showed as much improvement in two or three days after such therapy as patients with similar lesions may display in two weeks under ordinary chemotherapy. No appreciable effect on the quantitative Wassermann reaction was noted.

Four of 5 patients who did not receive subsequent chemotherapy within four months had mucocutaneous relapses. The fifth patient retained a positive Wassermann reaction but apparently had no relapse. The 3 other patients were given routine chemotherapy within two weeks after the administration of fever therapy.

The febrile state destroys a large number of spirochetes, yet enough survive in the coolor parts of the body to cause relapses. The spirocheticidal action of the febrile state may prove to be of value when used concurrently with chemotherapy.

MALIGNANCY AND LYMPHOGRANULOMA VENEREUM. A. V. DIEBERT and R. B. GREENBLATT, Am. J. Syph., Gonor. & Ven. Dis. **26**:330 (May) 1942.

The authors report a case of epidermoid carcinoma of the vulva in a patient 24 years of age with a chronic rectal stricture and elephantiasis of the clitoris and the labium. The occurrence of a malignant lesion with lymphogranuloma venereum is too frequent to be purely coincidental.

SYPHILIS OF THE SPINAL CORD. A. B. KING, Am. J. Syph., Gonor. & Ven. Dis. **26**:336 (May) 1942.

The author describes seven easily distinguishable, distinct clinical entities as a result of syphilis of the spinal cord. These are vascular occlusions, meningomyelitis, Erb's spastic paraplegia, progressive muscular atrophy, gumma, hypertrophic cervical pachymeningitis and tabes dorsalis. To this last may be added the damage that is occasionally sustained by the cord following arsphenamine therapy.

Large vascular accidents involving the spinal arteries are an unusual condition. The signs of thrombosis of the anterior spinal artery are a segmental loss of pain, fever and other manifestations of injury to the anterior horn cells, with varying amounts of damage to the ascending spinothalamic and descending pyramidal tracts. The acute paraplegias of syphilis are also due to vascular occlusions.

A diffuse meningomyelitis is seen early in the disease. Pain, due to root irritation, is a frequent feature. The upper thoracic portion of the cord is most often affected, and girdle pains are characteristic.

Erb's spastic paraplegia is a late form of syphilitic myelitis. Besides the spastic paraplegia, there are frequently bladder disturbances.

Progressive muscular atrophy is also a late complication. The anterior horn cells are the principle site of injury. The lower cervical portion of the cord is the most frequent location for this variety of syphilis of the spinal cord. Muscular atrophy and fasciculations are the usual clinical findings.

Gummas may occur after the first year of infection. The signs are those of neoplasm of the cord.

Tabes dorsalis is a process in which the sensory roots alone are damaged, resulting in ataxia, loss of reflexes, bladder disturbances, characteristic gait and various forms of pain. One or several cranial nerves may be injured concurrently. While the site of the lesion is clear, its mode of production is not. It is not unusual to find the serologic reactions of the blood and spinal fluid negative.

Hemorrhagic myelitis is included because it may be a complication of arsphenamine therapy. Arsenic alone is probably responsible for the damage to the cord. The lesion is essentially capillary damage produced by arsenical drugs, which results in remote hemorrhages in the substance of the cord. Usually the patients sustain a complete transverse myelitis.

REUTER, Milwaukee.

SYPHILIS: REVIEW OF RECENT LITERATURE. CHARLES F. MOHR, PAUL PADGET, RICHARD HAHN and JOSEPH EARLE MOORE, Arch. Int. Med. **69**:470 (March) 1942.

Mohr and his associates present a 75 page review of selected material published between July 1940 and November 1941. It is likely that every dermatologist will discover in this review worthy articles which have failed to come to his attention. In most instances the abstracts are accompanied by editorial comment.

LYNCH, St. Paul.

SYPHILIS IN OPHTHALMOLOGY. E. W. ASSINDER, Brit. J. Ophth. **26**:1 (Jan.) 1942.

This is the Middlemore Lecture for 1941. The subject of syphilis in ophthalmology is presented from the viewpoint of a nonophthalmologist, and the article does not lend itself well to abstracting.

The total number of persons given the Wassermann test was 6,839. Of these, 1,015 gave a positive or weakly positive reaction. The number of positive reactions in 1940 was less than one third of that in 1928.

There were 19 patients with gumma in the orbital area. Tumors of the orbit demand an examination of the blood as one of the first examinations in a differential diagnosis. There were 17 patients with scleritis and episcleritis. The process is gummatous.

Of the 553 patients with keratitis, the majority had the diffuse interstitial type. About 97 per cent had the congenital variety. Of 100 consecutive patients with keratitis of the congenital type, 85 gave a positive Wassermann reaction; 14 of the 15 who gave a negative reaction had had previous antisyphilitic treatment. Injuries of all kinds and pregnancy may be exciting causes of the keratitis. In 43 per cent the keratitis was limited to one eye. The average age at onset of the patients with the congenital type was 18 years. Of 100 patients, 65 had peculiarities of the teeth and physiognomy and 10 were deaf. The arsphenamine compounds and bismuth are the best drugs in the treatment of syphilis. Assinder is convinced that hot fomentations prolong the florid stage of keratitis and result in denser corneal scars.

There were 96 patients with iritis, including cyclitis. No child under 1 year of age had iritis. In 15 patients the iritis was associated with acute syphilis. There were 87 patients with choroidoretinitis; in the great majority it was of congenital origin. There were 74 patients with optic nerve atrophy, 19 with optic neuritis and 119 with nerve palsies, including Argyll-Robertson pupils.

The process in locomotor ataxia is slow strangulation of the nerve fibers and the vessels in the nerves, combined with arteritis, causing perivascular scarring and thickening, with resulting atrophy of the nerve cells in the retina leading to atrophy of the fibers as shown at the disk, which leads to the question: "Is the atrophy of the disk really primary?" W. ZENTMAYER. [ARCH. OPHTH.]

APPLICATION OF HIRST'S PHENOMENON TO THE TITRATION OF VACCINIA VIRUS AND VACCINIA IMMUNE SERUM. F. P. O. NAGLER, M. J. Australia **1**:281 (March 7) 1942.

In July 1941 Hirst described the phenomenon of agglutination of red cells by allantoic fluid of chick embryos infected with influenza virus. The author confirmed this work and then applied similar methods to vaccinia virus, which he found to have a similar effect on the red blood cells of the fowl. He described in detail his method of growing the virus on the chorioallantoic membrane of ten day chick embryos and then concentrating it to such an extent that agglutination with the red blood cells of hens was produced with a dilution of 1:256. Antibodies in rabbit and human serum following vaccination were then demonstrated and quantitatively estimated by virus-neutralizing potencies.

These experiments offer a more available and sensitive test than the mouse intracerebral method, which had hitherto been the only satisfactory means of estimating the immunologic response to vaccination other than revaccination at various times afterward. The use of the agglutination test also provides a rapid determination of the potency of materials prepared for vaccination.

INDUSTRIAL DERMATITIS. H. LEIGHTON KESTEVEN, M. J. Australia **1**:406 (April 4) 1942.

Industrial dermatitis has become much more frequent in Australia since the great increase in the number of factory workers brought about by war activities has put thousands of men and women into occupations which are strange to them. They do not, as under normal conditions, become quickly familiar with all the risks, minor and major, of the occupation, and there is therefore at present a large increase in occupational invalidities, traumatic and otherwise.

Two types of industrial dermatitis are described: uncomplicated and complicated. Uncomplicated industrial dermatitis is considered to be that caused by contact of the skin with a strong cutaneous irritant, such as solution of potassium hydroxide (caustic potash), also called a "corrosive" injury to the skin. Most conditions of this kind clear up spontaneously in three or four weeks unless the damage is deeply seated because of long-continued contact with the irritants, such as an erythema due to methenamine, which is slowly acting and has great penetrability. In such cases of uncomplicated industrial dermatitis, the sufferer can usually be removed to some other work in the same factory, which will prevent the injury from disabling him as regards his war effort.

Complicated industrial dermatitis is that resulting from the action of three factors. 1. *Individual Sensitivity.*—It is the common experience of every industrial medical officer that certain substances with which many men in the factory constantly come in contact do from time to time give rise to more or less intensely irritating eruptions. The majority of these conditions are noted among new workers. In these cases the prognosis on return to work is usually fairly good. Almost without exception, however, those in whom sensitivity develops after long periods of exposure will never again acquire a tolerance. 2. *Want of Cleanliness.*—With no other contributing factor this can be productive of a pustular rash over any area of the body likely to be rubbed. It is seen particularly among workers in engineering shops who are apt to get oil on the arms and legs. Erythematous papules and pustules are prone to occur. If due to Staphylococcus albus alone,

the condition remains localized to the areas exposed. If, however, Staphylococcus aureus appears in some of the papules or pustules, the condition changes rapidly to a true furunculosis, which may extend to nonexposed areas of the skin. This so-called oil dermatitis never develops on clean skin, and conscientious cleansing will avoid its recurrence. 3. *Superimposed Infection.*—This has already been discussed under the previous heading, but the author believes that preexisting dermatitis may predispose to development of an industrial dermatitis and, conversely, that some forms of seborrheic dermatitis, etc., are the result of neglected mild chronic occupational dermatoses.

The most important generalization from the war effort angle is that occupational dermatitis is not disabling. If this is not recognized, valuable trained labor will be wasted.

FRUMESS, Denver.

STUDIES OF PELLAGRA IN CHOSEN: IV. GASTRIC JUICE AND LIVER FUNCTION IN PELLAGRA. K. URABE, Jap. J. Dermat. & Urol. **48**:107 (Nov. 20) 1940.

Fifty-three cases of pellagra were observed between April 1939 and July 1940, and 42 of these were studied with regard to gastric juice and liver function. The majority of the patients showed gastric anacidity or hypoacidity and disturbance of the liver function. One patient was examined post mortem, and histopathologic changes were found in the liver. The author believes that there is a causative relation between the disturbance of the liver and pellagra.

A CONTRIBUTION TO THE NEVUS SYRINGOCYSTADENOMATOSUS PAPILLIFERUS. I. YAMASAKI, Jap. J. Dermat. & Urol. **48**:109 (Nov. 20) 1940.

The author reports the first case of naevus syringocystadenomatosus in Japan, that of a man aged 48 who since birth had in the right temporal region a brownish slightly raised tumor, 3.5 by 2 cm. It was of firm consistency and had a verrucous surface. On histologic examination different changes were found which are observed in lesions described as naevus syringocystadenomatosus papilliferus, naevus epitheliomatosus sebaceus, naevus sebaceus, epithelioma adenoides cysticum and epithelioma sebaceum. The fact that so many changes are found in the same lesion strengthens the opinion of Arzt and Kumer that all these tumors originate from the primitive epithelial layer.

STUDIES ON PELLAGRA IN CHOSEN: V. BLOOD FINDINGS IN PELLAGRA. K. URABE, Jap. J. Dermat. & Urol. **48**:117 (Dec. 20) 1940.

The author studied the blood in 49 cases of pellagra and made the following observations: The number of erythrocytes diminished at the height of the illness and increased gradually with the clinical improvement. The hemoglobin content and the color index were mostly diminished, while the leukocyte count was mostly increased. The only abnormal changes in the blood of 19 patients with pellagra were slight lymphocytosis and eosinophilia.

RESULTS OF INVESTIGATION OF THE POISON OF CIMEX LECTULARIUS. S. YAGI, Jap. J. Dermat. & Urol. **49**:1 (Jan. 20) 1941.

Using the extract of bedbug poison as an antigen, the author studied the complement fixation reactions of the serums of 150 subjects, including normal persons and persons suffering from bedbug bites. Of 47 who gave a positive reaction, 37 were suffering from bedbug bites. All the others who gave a negative reaction did not suffer bites. Two per cent of the subjects seemed to be insensitive to the bite of this insect. Most of those who had been repeatedly bitten showed a weak cutaneous reaction; some of these did not react at all. The percentage of the complement fixation reaction, however, was increased in those who showed a

weak cutaneous reaction after repeated bedbug bites. One patient who showed a positive cutaneous reaction after the injection of bedbug poison extract had generalized urticaria, which disappeared after ten hours.

ACNE-LIKE ERUPTIONS PRODUCED BY INDUSTRIAL FATS AND OILS: III. REVIEW OF THE LITERATURE AND ETIOLOGIC CONSIDERATIONS. Y. NAKAUCHI, Jap. J. Dermat. & Urol. **49**:3 (Jan. 20) 1941.

The author believes that acne-like eruptions produced by coal oil, trichloronaphthalene or tetrachloronaphthalene are due to the mechanical and chemical irritation produced by the tiny particles or droplets. When these particles are larger than the diameter of a hair follicle or a sweat pore they stay on the surface of the skin and produce dermatitis. When they are smaller they penetrate into the hair follicles, sebaceous glands and sweat glands. Other factors which play a role in the pathogenesis of these eruptions are the solubility of the irritants, the dilatability of the follicle ostium and the extent to which these irritants are rubbed into the skin during work. Follicular keratosis and occasionally also keratosis of the sweat pore may develop alone or in association with dermatitis. When the irritating particles penetrate only the upper portion of the follicle lichen pilaris is produced; when they penetrate deeper retention atheromas develop. These and the subcutaneous abscesses usually do not contain bacteria. The abscesses are probably produced by breaking through of the contents of small sebaceous glands into the connective tissue of the corium. Thus, one finds abscess formation, granulation tissue with or without giant cells, horny fragments and tiny particles or droplets of the irritating substances.

TRICHOPHYTON INFECTION IN FORMOSA: II. FUNGOUS INFECTION OF THE SCALP IN CENTRAL FORMOSA. S. TAKAHASHI and T. YOH, Jap. J. Dermat. & Urol. **49**:23 (March 20) 1941.

In 947 cases of superficial tinea infection of the scalp in public schools in central Formosa 992 positive cultures were obtained. There were 583 cultures of Microsporon ferrugineum (Grubyella ferruginea), 311 of Trichophyton violaceum, 31 of Trichophyton glabrum and 67 of Trichophyton coccineum. In 7 cases of tinea profunda of the scalp M. ferrugineum was obtained. Thus M. ferrugineum is the most frequent agent in tinea capitis in central Formosa as well as northern Formosa, while T. violaceum is much more frequent in central than in northern Formosa.

In 3 cases in which M. ferrugineum was cultured and in 1 case in which T. glabrum was cultured a mixed infection with Achorion schoenleinii was present, while in 1 case in which T. glabrum was cultured Achorion formosaensis was also found. In 40 other cases there was mixed infection of M. ferrugineum and T. violaceum.

STUDIES OF PELLAGRA IN CHOSEN: VI. CUTANEOUS MANIFESTATIONS AND HISTOLOGIC FINDINGS IN PELLAGRA. K. URABE, Jap. J. Dermat. & Urol. **49**:24 (March 20) 1941.

The author reports 4 cases of pellagra in which there was, in addition to the usual cutaneous lesions, the so-called Casal ring on the neck. Microscopic examination showed in the erythematous stage edema, capillary dilatation and slight infiltration with plasma cells in the papillary layer and thinning of the prickle cell layer. In the bullous and ulcerative stage there were edema of the spinous layer, pyknosis of the nuclei of the prickle cells, small and large vesicles, loosening of the connection between the corium and the epidermis, lifting of the epidermis and ulcer formation with crusting. In the stage of pigmentation there were dilatation of the capillaries, hyperkeratosis and parakeratosis of the epidermis and hyperpigmentation of the basal cell layer.

Society Transactions

METROPOLITAN DERMATOLOGICAL SOCIETY

MAURICE J. COSTELLO, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Oct. 20, 1941

Rosacea with Keratitis. Presented by DR. ROYAL M. MONTGOMERY.

A. L., a man aged 53, has had the present eruption on the cheeks for fifteen years and on the forehead for four months. The right eye has been affected for five years.

The skin of the cheeks and forehead is erythematous and telangiectatic, with a moderate number of small pustules. There is some scarring. The right cornea is covered with a gray scar, especially the outer two thirds. There is apparently a beginning invasion of the left cornea.

The patient has had an operation on the right eye, without apparent success. The Wassermann reaction of the blood was negative. Roentgenograms showed some involvement of the frontal and ethmoid sinuses and the antrums.

The patient had been referred to the dermatologic clinic for treatment of the eruption. There it was diagnosed as keratitis from rosacea. Treatment has consisted of administration of dilute hydrochloric acid internally and application of white lotion of twice N. F. strength externally. He has had 75 r of unfiltered roentgen rays applied to the face.

DISCUSSION

DR. LAIRD S. VAN DYCK: Keratitis with rosacea is believed to be due to a riboflavin deficiency. Conjunctivitis and keratitis in cases of rosacea are, according to reports, not uncommon, but perhaps frequently overlooked if the ocular involvement is slight. The keratitis usually improves when riboflavin is administered in doses of 3 mg. two or three times a day.

DR. MAURICE J. COSTELLO: I agree with Dr. Van Dyck. The association of keratitis and blepharoconjunctivitis with rosacea is not uncommon. Dr. Cole believes that riboflavin and hyperthermy are the most effective treatment for syphilitic interstitial keratitis. I think that riboflavin therapy would benefit this patient.

DR. THOMAS N. GRAHAM: I agree with Dr. Costello and Dr. Van Dyck. I believe that keratitis with rosacea is seen more often in ophthalmic clinics than in dermatologic clinics, probably because the cutaneous lesions are of less importance to the patient and because the ocular involvement, unless advanced, is frequently overlooked by the dermatologist.

DR. RICHARD J. KELLY: This is not unlike a case I presented at a meeting a year ago. The patient was a woman of 48 or 50 years, with severe rosacea, much like the Lewandowsky type. I gave her ultraviolet irradiation and biweekly injections of old tuberculin in a dilution of 1:100,000. There was a remarkable improvement in three months. Today she is completely cured.

DR. LESLIE P. BARKER: Keratitis associated with rosacea is seen infrequently in dermatologic clinics, although there have been a few cases at Vanderbilt Clinic. The administration of riboflavin internally and treatment of the rosacea generally and locally certainly offer the best treatment for the keratitis.

DR. ANTHONY C. CIPOLLARO: Keratitis complicating rosacea is rare from a dermatologic standpoint. My experience in clinics and private practice does not

extend over many years, and during this time I have rarely encountered a case. Patients with rosacea in the dermatologic clinics are not examined for keratitis. The ophthalmologists treating keratitis undoubtedly see an accompanying rosacea much more often.

DR. ROYAL M. MONTGOMERY: I agree with Dr. Cipollaro. Rosacea with keratitis has been recognized for a long time but is seen only rarely in dermatologic clinics. Schamberg reported a case in 1913 (*J. Cutan. Dis.* **31**:504 [July] 1913). The patient has already been given riboflavin, 6 mg. daily for two months. Ophthalmologists believe that treatment of rosacea prevents further spread of the keratitis.

Chronic Lymphangitis of the Face. Presented by DR. ANTHONY C. CIPOLLARO.

H. M., a man aged 23, born in the United States, stated that the eruption began seven years ago with sudden swelling of the eyelids and the forehead in the region of the glabella. It has not changed since its inception. The patient stated that he had never had erysipelas or any other infection and that he had no illness at the time this began. He arose one morning and noticed that swelling was present. His tonsils were removed twenty-two years ago.

He is in good general health and has been examined in the medical department of the New York Post-Graduate Hospital, as well as in the vascular disease and otolaryngologic departments, without any definite pathologic changes being noted. Roentgenograms of the skull and chest showed no abnormality. The basal metabolic rate on two occasions showed —8 per cent. The stool was negative for parasites. The Wassermann reaction of the blood was negative, and the urine was normal. Blood counts on several occasions were normal. The results of chemical examination of the blood and sugar tolerance tests were also normal. The Frei test gave a normal result.

The patient has had various types of treatment, including sulfanilamide, and nothing seemed to influence the eruption. He has just had his fourth roentgen ray treatment, consisting of filtered radiation through 3 mm. of aluminum and a kilovoltage of 135. Each treatment consisted of 137 r. There seems to be some amelioration of the eruption about the forehead as a result of the roentgen treatments.

The patient is presented for suggestions as to the possible etiologic agent and as to therapy.

DISCUSSION

DR. LAIRD S. VAN DYCK: I noticed a great deal of swelling of the eyelids and forehead. I should call the disease a chronic lymphedema.

DR. MAURICE J. COSTELLO: At one of the previous meetings I presented a patient with solid edema of the ears of four years' duration. He was admitted to Bellevue Hospital and treated with sulfanilamide. He was given 60 grains (4 Gm.) the first day, 40 grains (2.6 Gm.) the second and 30 grains (2 Gm.) daily subsequently. The result was remarkable. This drug was administered for a long period without any ill effects. If sulfanilamide therapy has not been tried on this patient, I certainly suggest that it be given a fair trial.

DR. ANTHONY C. CIPOLLARO: The patient has had sulfanilamide. He received 60 grains a day for three or four days and then 30 grains a day for several weeks. There has been no improvement with chemotherapy. He improved with roentgen therapy, and if this improvement continues I shall present him again.

Staphyloderma; Ecthyma? Presented by DR. THOMAS N. GRAHAM.

J. N., a white man aged 33, first had a small, pustular, crusted lesion on the flexor surface of the left leg, just above the ankle, which developed in January 1941. A shallow ulceration developed within the next few weeks, and the lesion extended peripherally to become oval, about 2 cm. in diameter. The ulcer healed, and the lesion became elevated and indurated and presented small perforations

from which there exuded an amber-colored serous fluid, which formed a dry crust. Biopsy was done on March 21; Dr. Else Barthel gave the following observations: "The section shows acanthotic epidermis that is very thin in one area. In this area the epidermis is atrophic and round cells have wandered between the cells. The corium is filled with a number of new engorged blood vessels, inflammatory exudate and large pale-staining cells, as well as islands of epidermal cells which apparently belong to follicles." She suggested a diagnosis of granuloma pyogenicum.

Roentgen therapy and local treatment with ammoniated mercury ointment and bacteriophage ointment were ineffective. The lesion continued to increase in size and was excised by surgical diathermy on April 11. Healing was uneventful.

Before the wound was completely healed, several small similar lesions appeared on the legs. These started, as had the original lesion, with a small pustular, crusted papule, and despite vigorous treatment they increased in size. Treatment has consisted of application of ammoniated mercury ointment, 2 per cent aqueous solution of gentian violet, tar ointment, 10 per cent silver nitrate solution, 5 per cent sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) ointment, chlorhydroxyquinoline ointment and 10 per cent iodochloroxyquinoline in petrolatum. The patient was also given sulfathiazole internally, 7½ grains (0.5 Gm.) three times a day for two weeks. Roentgen therapy and ultraviolet irradiation were both employed. Some of the lesions were curetted and desiccated, but they always recurred at the edge.

Medical examination showed nothing abnormal except a basal metabolic rate of —13 per cent, for which the patient was given thyroid. In order to build up his general resistance, he was given injections of liver and oral doses of vitamins. The Wassermann reaction of the blood was negative, and the urine was normal. Mycologic examination showed no growth. Culture of material from a lesion showed Staphylococcus aureus.

DISCUSSION

DR. LESLIE P. BARKER: There is certainly no evidence of ecthyma at present. I believe this patient has a rather common but stubborn type of eczema, sometimes referred to as eczematoid dermatitis and often due to foci of infection. I suggest a complete physical examination, with a thorough search for foci of infection and a trichophytin test. Locally 10 per cent carboneol in acetone or carbon tetrachloride is often effective.

DR. ROYAL M. MONTGOMERY: I agree with Dr. Barker that a trichophytin test should be performed and further mycologic studies made. I favor a diagnosis of dermatophytid rather than a primary infection.

DR. LAIRD S. VAN DYCK: I should call the condition a nummular or orbicular eczema.

DR. MAURICE J. COSTELLO: I believe that he has a nummular eczema. I advise the application of coal tar ointment, with dressings changed every forty-eight hours. It should be wiped off gently with liquid petrolatum or olive oil. This treatment and the application of roentgen rays are the best form of therapy.

DR. THOMAS N. GRAHAM: I think that it is impossible to make a diagnosis in this case based on the appearance of the patient tonight. Since I last saw him there has been great improvement. I believe the condition is a staphyloderma, and clinically in many respects it seems to fit in with ecthyma. The peripheral extension of the lesions, their response to iodochloroxyquinoline and chlorhydroxyquinoline ointments and the microscopic picture I believe rule out orbicular eczema. The trichophytin test is not to be relied on in making a diagnosis of dermatophytosis, and mycologic studies have showed no organisms.

DR. FRANLIN H. GRAUER: I agree that mycologic studies should be made. If they give negative results, I should consider this case to be one of nummular or orbicular eczema, even though there were no lesions on the dorsal surfaces of the hands or on the arms. With regard to therapy, since the roentgen rays have been ineffectual I should try a high vitamin diet, coal tar ointment, general ultraviolet irradiation and possibly calcium internally.

ANTHONY C. CIPOLLARO, M.D., *President*
MAURICE J. COSTELLO, M.D., *Secretary*

Nov. 17, 1941

Leather Dye Dermatitis. Presented by DR. LESLIE P. BARKER.

L. V., a man aged 40, has had an eruption for eleven months. It began on the dorsum of the right big toe following an injury. It remained localized in a small area for about a month and then spread proximately and also involved the opposite foot. It has always spread with a rather definite border and has never been between the toes, on the soles or on any other part of the body. Recently he has had eighteen to twenty roentgen ray treatments. He had a similar attack nine years ago that lasted about six months; no causative agent was found.

On both feet, especially on the dorsa extending up almost to the ankle, is a well demarcated, erythematous, oozing and crusted dermatitis. Some of the dermatitis extends around to the sides of the feet. There is a suggestion of atrophy of the skin and subcutaneous tissues of the toes of the right foot. The reaction to a patch test with 2 per cent paraphenylenediamine in petrolatum was negative and to one with leather also negative.

DISCUSSION

DR. ROYAL M. MONTGOMERY: I agree with the diagnosis. This condition is greatly aggravated in warm weather. I think a patch applied closer to the eruption is more apt to elicit a positive reaction. I suggest that the patient have shoes made to order without a leather lining. This is essential for a permanent result.

DR. MAURICE J. COSTELLO: I think that Dr. Barker has proved the diagnosis. The best treatment is elimination of the causative irritant.

DR. LAIRD S. VAN DYCK: I agree with the diagnosis. I suggest that the patient wear canvas shoes.

DR. EUGENE F. TRAUB (by invitation): There seems to be little question but that Dr. Barker has proved his case to be one of dermatitis, and clinically, from the appearance, this seems to be the logical diagnosis.

DR. LESLIE P. BARKER: This patient had received more than twenty roentgen ray treatments on the feet. He is trying to get a pair of shoes which are made of fabric, but he finds it rather difficult. The wearing of white cotton socks during the past three months has apparently produced no improvement.

Basal Cell Epithelioma Successfully Treated with Roentgen Rays. Presented by DR. JOSEPH C. AMERSBACH.

G. M., a woman aged 43, has had an eruption for six years. It began as a small red macule on the inner canthus of the eye. The patient thought it was an irritation due to eyeglasses. Four years ago she was advised to have treatment with a quartz mercury vapor glow lamp. She received this off and on for three years. There was no treatment for a year prior to her admission to the New York Skin and Cancer Hospital in June 1941.

When she entered the hospital there were diffuse thickening, crusting and ulceration involving more than half of the left upper eyelid and about seven eighths of the lower lid, extending medially to the midline of the bridge of the nose and extending within the orbit along the inner aspect of the eyeball.

The microscopic diagnosis was "embryonic type of epithelioma."

The patient was referred to the tumor clinic for consultation, and probable removal of the eyeball was advised. Since the sight of the eye was not impaired and the eye showed only a conjunctivitis due to the ectropion produced by the malignant lesion, it was decided to treat the patient with roentgen rays. A lead shield was placed over the eyeball, and the involved area was treated, the focal point being the inner canthus. The total dosage was 4,000 r. The first dose of

750 r was given unfiltered. The remaining treatments, given at weekly intervals, were with rays filtered through 3 mm. of aluminum.

DISCUSSION

Dr. Laird S. Van Dyck: I want to congratulate the presenter on his success in the treatment of this lesion. It was a splendid result in a difficult case.

Dr. Eugene F. Traub: I can only second Dr. Van Dyck's remarks. Conditions like that in this case are difficult to manage and frequently require a combination of different methods for satisfactory treatment. Irradiation, as proved in this case, is generally the method of choice and sometimes may be successfully used in conjunction with previous desiccation and curettement of the portions of the lesion difficult to manage by roentgen therapy alone. Surgical excision is the last resort in these cases but sometimes yields excellent results after repeated plastic operations, which, however, usually require hospitalization. The excellent result in this case was achieved without hospitalization or repeated operations.

Dr. Leslie P. Barker: I think this is a remarkable result from radiotherapy. In a similar case I gave 400 r in daily doses until a total of 8,000 r was reached and the result was excellent. In this case I should prefer roentgen therapy to surgical intervention.

Dr. Richard J. Kelly: This type of lesion is believed by surgeons not to belong in the field of dermatology. I think this patient has less ectropion than there would have been if the lesion had been removed surgically.

Dr. Franklin H. Grauer: I agree with the previous speakers that this is an excellent therapeutic result.

Dr. Anthony C. Cipollaro: This case aroused much interest because of the extensiveness of the lesion and its proximity to the eye. Some of the consultants expressed the opinion that the lesion was inoperable. The patient is now clinically cured. The arrest of the process was accomplished with comparatively low voltage roentgen rays and little filtration. Approximately 4,000 r was applied over a period of five weeks.

Dr. Joseph C. Amersbach: Dr. Cipollaro covered most everything. A close cooperation between the surgeon and the dermatologist is essential, because not only may certain important phases of treatment be arranged but, as in this case, with absence of such cooperation therapy may be inadequate because of improper diagnosis.

Hypovitaminosis Resembling Pityriasis Rubra Pilaris. Presented by Dr. Laird S. Van Dyck.

K. S., a housewife aged 60, was first seen one week ago with an eruption on the arms and back of three months' duration. She has been on a diet for peptic ulcers since 1923 and has also been treated for colitis and hyperthyroidism.

Examination shows an acuminate, follicular, papular eruption with a tendency to form irregular, yellowish red, poorly defined patches on the arms and back. The skin is abnormally dry. Many of the papules are spiny. There is no hyperkeratosis of the palms or soles. She has not noticed any night blindness. Her diet appears to have been greatly deficient in vitamin C but approximately normal in vitamin A content. She shows evidence of hyperthyroidism, such as swelling of the neck, nervousness and rapid pulse.

DISCUSSION

Dr. Eugene F. Traub (by invitation): There is some question in my mind as to whether this eruption is due to a vitamin deficiency. However, it would be a relatively easy matter to determine that. One might treat the lesions locally with resorcinol or ammoniated mercury for a few weeks, and if there should be no improvement as a result of local therapy, then vitamin therapy might be instituted. Another method of proceeding might be to give vitamins alone without any local

treatment. This patient also presented an eruption on the face which suggested a beginning rosacea. I hope Dr. Van Dyck will be able to prove whether or not there is a relation to vitamin therapy.

DR. FRANKLIN H. GRAUER: Morphologically this eruption falls into the group of lichen spinulosus and as such must be differentiated from pityriasis rubra pilaris. Etiologically speaking, however, I believe that the condition in this case may be a good example of vitamin A deficiency. This patient certainly has the necessary systemic background for a deficiency disease: colitis, a peptic ulcer and hyperthyroidism. She may be receiving an adequate diet, but because of any one or a combination of the aforementioned conditions there may be failure to assimilate or properly utilize the vitamins ingested.

DR. THOMAS N. GRAHAM: I agree with Dr. Grauer. The clinical picture fits in with the eruptions which have been described as being due to a vitamin A deficiency. I suggest that a biophotometer test be done and the vitamin A and carotene content of the blood be determined.

DR. MAURICE J. COSTELLO: I think it possible that this patient has a hypovitaminosis. In treating the patient I should advise against intramuscular injections of vitamin preparations, as they may result in serious lowering of the blood level of vitamin A. I should give the vitamin orally.

DR. LAIRD S. VAN DYCK: There are three interesting points in this patient's background, any one of which could lead to vitamin deficiency. First, her peptic ulcer diet has obviously been lacking in vitamin C; secondly, her chronic colitis would tend to prevent absorption of adequate amounts of vitamins even though her diet contained the normal amounts, and, lastly, she suffers from hyperthyroidism, which raises the body's requirements, especially with reference to vitamin A, if one can accept the hypothesis that there is an antagonism between thyroxin and vitamin A.

A Case for Diagnosis. Iododerma? Presented by DR. RICHARD J. KELLY.

J. M., a man aged 48, was first seen four weeks ago. At that time he presented an indolent eruption on the dorsum of the left hand, which had been present for three months. It consisted of central scarring with raised granulations toward the margin of the lesion. The diameter was approximately 4 cm. There was no complaint of pain. There was no history of syphilis or of ingestion of drugs, particularly of bromides and iodides. The patient is a chauffeur by occupation. He stated that he had had no contact with plants.

Physical examination revealed no regional adenopathy. He stated that he had been having eight to ten highballs daily for a period of four months. The Wassermann reaction of the blood and the reaction to a Kline test were negative. Biopsy, culture and microscopic examination for fungi gave negative results.

DISCUSSION

DR. EUGENE F. TRAUB (by invitation): It is rather difficult to arrive at a diagnosis in this case. In favor of the diagnosis of iododerma or bromoderma is the patient's history of bromide ingestion a number of years ago. Frequently, patients have iododerma or bromoderma some time after they have apparently stopped taking the drug. This is because a certain amount of these drugs is regularly obtained in the daily food ingested. I recall a case in which the patient, hospitalized and on a carefully supervised diet presumably free from iodides and bromides, failed to improve and it was subsequently found that the microscopic amounts of bromide in the white bread the patient was getting might have been sufficient to keep the eruption active. It is possible, therefore, that the patient presented tonight is getting a sufficient amount of iodide or bromide, and this should be excluded, if possible, while at the same time other diagnoses are still considered.

DR. FRANKLIN H. GRAUER: I agree with Dr. Traub. I suggest a therapeutic test consisting of increased ingestion of sodium chloride and intravenous administration of physiologic solution of sodium chloride. The vegetative fungating type of bromoderma may undergo involution slowly, and the roentgen rays frequently are a useful therapeutic adjuvant.

DR. LAIRD S. VAN DYCK: If the patient were a woman I should say the eruption was dermatitis factitia clinically and apply an occlusive dressing.

DR. MAURICE J. COSTELLO: My first diagnosis would be pyogenic dermatitis. Iododerma has also to be considered. The vegetating type of bromoderma is seen mostly on the legs. I suggest that sulfathiazole ointment be tried.

DR. ANTHONY C. CIPOLLARO: I am not certain that the clinical features substantiate the diagnosis of iododerma. Further observation and study are required before one can arrive at the correct diagnosis.

DR. RICHARD J. KELLY: The patient gave a history of ingestion of bromide five years ago. He admitted using and liking large amounts of salt. Sections showed chronic granuloma. Cultures for fungi were negative. The patient stated that the new lesion on the right hand cleared with use of a boric acid ointment.

Cheilitis Glandularis. Presented by DR. LAIRD S. VAN DYCK.

A. S. C., a Spanish seaman aged 42, was first seen on Sept. 19, 1941 with an inflamed and swollen lower lip of two years' duration. He had had two courses of roentgen therapy at a hospital in San Francisco, eighteen months ago and one year ago respectively. Six months ago he was treated at a hospital in Montreal, Canada, with silver nitrate cauterization and cod liver oil ointment and was told that he had a roentgen ray burn.

Examination showed a general swelling of the lower lip with scaling and crusting. When the scales were wiped off, droplets of mucoid glairy fluid appeared on the surface of the mucous surface of the lip. There was a circumscribed, thick, crusted area 5 mm. in diameter on the left side of the lower lip. This crust was tightly adherent to the underlying tissue and could not be removed without producing ulceration. There was no apparent atrophy or telangiectasia.

There has been no response to therapy with all kinds of ointments and other local treatment. There seemed to be temporary improvement for two weeks after the administration of nicotinic acid amide and vitamin B complex.

The Wassermann reaction of the blood has been repeatedly negative.

DISCUSSION

DR. MAURICE J. COSTELLO: I agree with the diagnosis. On pressure there are droplets of oil seen on the mucous membranes.

DR. EUGENE F. TRAUB (by invitation): One encounters cases like this so seldom that it is difficult to speak of characteristic features, but in the few cases I recall there was considerable thickening of the lower lip and the large patent duct opening could be readily seen. In this case the mucosa has been damaged, these opened ducts are not visible and it is difficult to decide whether the exudation is not coming from the eroded mucosa. I have never observed a case in which cheilitis glandularis and cheilitis exfoliativa were present at the same time, and I doubt that this does occur. This case must be studied further before the diagnosis of cheilitis glandularis can be established.

DR. LAIRD S. VAN DYCK: Histologic examination of a section taken from the keratotic lesion on the left side of the lip showed "preepitheliomatous hyperkeratosis, possibly very early epithelioma."

Pyoderma Gangraenosum in a Patient with Syphilis. Presented by DR. MAURICE J. COSTELLO.

I. N., a Negress aged 23, stated that about ten years ago she bruised her right leg and the area became progressively ulcerated. The ulcer failed to heal, and

the patient consulted a physician, who told her that she had "bad blood." She was given "shots" in the hip and arm, but the ulcer did not heal. She went to a different physician, who treated the ulcer locally; it healed but soon "broke down." She has received weekly injections in the hip and arm for the past four years.

Examination revealed an oval ulceration on the anterior surface of the lower third of the right leg, about 2 inches (5 cm.) in diameter, with exuberance of granulation tissue and surrounded by an area of scar tissue.

DISCUSSION

DRS. EUGENE F. TRAUB (by invitation), FRANKLIN H. GRAUER, THOMAS N. GRAHAM and LAIRD S. VAN DYCK agreed with the diagnosis.

Pellagra in Unusual Locations. Presented by DR. MAURICE J. COSTELLO.

H. J., a Negress aged 31, stated that for the past three or four months she has been indulging in alcoholic beverages excessively, with much neglect of usual meals. About one month ago, the patient first noticed chafing and burning around the genitalia, some soreness of the mouth and dysphagia. She had diarrhea prior to her admission to Bellevue Hospital.

The lips were dry and cracked and the tongue angry red and excoriated in places. There were large, round, excoriated, oozing lesions beneath each breast. There were much oozing, crusting and erythema of the intergluteal and vulval regions. There was fissuring, scaling, crusting and depigmentation on the dorsa of the hands. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. LAIRD S. VAN DYCK: The lesions on the hand were characteristic. I have never before seen lesions on the breast.

DR. FRANKLIN H. GRAUER: I agree that this patient has typical pellagra. In some patients the cutaneous manifestations occur on other than exposed surfaces, namely, over points of pressure, in the intertriginous areas and on the scrotum. The feeling today is that not only sunlight, but any type of irritation may act as a precipitating factor in the development of the cutaneous lesions. The patient also presents a cheilosis with fissures at the angles of the mouth, which suggests a riboflavin deficiency in addition to pellagra. These lesions may not respond to supplements of nicotinic acid, and it may be necessary to give riboflavin in addition.

DR. RICHARD J. KELLY: I noticed numerous lesions on the back that were nodular.

DR. EUGENE F. TRAUB (by invitation): Does the presenter look on this patient's condition as pseudopellagra or a real pellagra, or is this distinction still made at Bellevue Hospital?

DR. MAURICE J. COSTELLO: Pellagra is often seen in the dermatologic wards of Bellevue Hospital in September or October. The patients suffering from this dermatosis give a history of ingestion of gin and cheap alcohol. They often have an associated diarrhea.

Multiple Gummas Successfully Treated by Oral Administration of Sodium Bismuth Triglycollamate. Presented by DR. MAURICE J. COSTELLO.

J. H., a white man aged 63, had a penile lesion about thirty years ago, for which he received medicine by mouth for two months. He did not receive any injections in the hip or arm. There is no history of gonorrhea or any other illness.

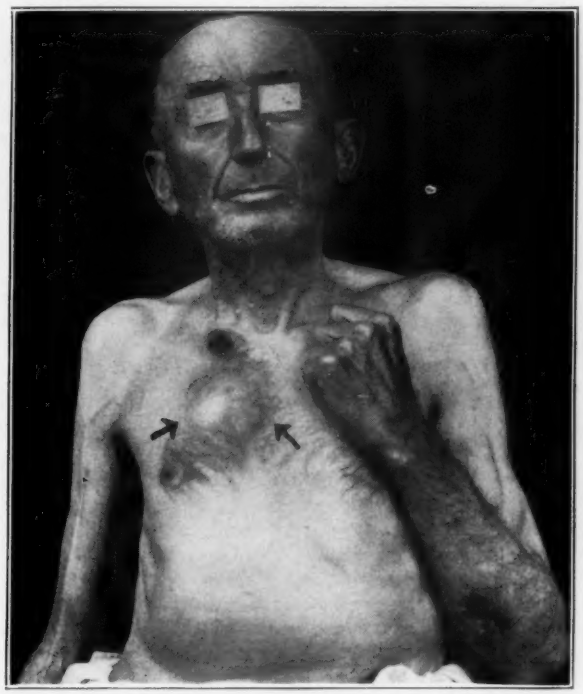
The patient first noticed an ulceration on the left forearm about three months ago, which became progressively larger. Two months later he noticed a swelling on the right side of the chest with ulceration above this area.

Examination revealed a punched-out oval ulcer about 2 by 1 inch (5 by 2.5 cm.) with an erythematous areola just beneath the right sternoclavicular articulation,

two large irregular ulcers near the left elbow, exuding a serosanguineous material, a firm and nontender tumor just beneath the ulcer in the sternoclavicular joint and a small swelling, about the size of a walnut, in the right temporoparietal region. The Wassermann and Kahn reactions of the blood were 4 plus, and the spinal fluid was normal. Treatment consisted of the administration of sodium bismuth triglycollamate, 150 mg. three times a day, after meals, which caused complete disappearance of all the lesions after a period of six weeks.

DR. LAIRD S. VAN DYCK: It is interesting to see such a good result from this type of therapy.

DR. FRANKLIN H. GRAUER: This demonstrates a satisfactory response to oral bismuth therapy.



Multiple gummas before oral administration of a bismuth compound.

MANHATTAN DERMATOLOGIC SOCIETY

DAVID L. SATENSTEIN, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

April 14, 1942

A Case for Diagnosis. Perivasculitis Nodosa Necrotisans? Presented by DR. MAURICE J. COSTELLO.

O. C., a Cuban woman aged 49, from the outpatient department of Bellevue Hospital, presents an eruption on the legs of one year's duration. It consists of quarter-sized to silver dollar–sized, hyperpigmented, indurated, plaquelike areas

of phlebitis. There are about nine lesions on each leg. They are irregularly distributed and increase in size and induration peripherally.

The disease becomes ameliorated by rest in bed for a long time. During one period of hospitalization, when the patient was confined to bed for six weeks, the eruption underwent definite involution.

A biopsy was inconclusive.

DISCUSSION

DR. GEORGE M. LEWIS: The age of the patient and the deep situation of the lesions would favor the presenter's diagnosis rather than erythema induratum.

DR. E. WILLIAM ABRAMOWITZ: Was there any histologic resemblance to sarcoid?

DR. ISADORE ROSEN: The clinical features suggest the type of inflammatory nodular lesions that one sees after the ingestion of bromides. This type of lesion may also be associated with rheumatism. An absolute diagnosis can be established only by histologic study.

DR. HERMAN SHARLIT: I too feel that the histologic picture will give the diagnosis. Clinically I am simply impressed that the local reaction is in the nature of a phlebitis.

DR. WILBERT SACHS: I believe that this patient has a variety of deep perivasculitis and not dermatitis nodosa necrotisans. There are superficial and deep types, and in the latter the larger vessels are involved. Perivasculitis is due not to a local but to a systemic disturbance, such as syphilis.

DR. MAURICE J. COSTELLO: This patient does not have diabetes, syphilis or tuberculosis. Occasionally patients are seen who present only one palm-sized plaquelike lesion on the inner aspect of the lower third of the leg. These indurated areas last indefinitely and are little influenced by therapy except rest in bed. If the lesions are palpated carefully one finds thrombophlebitic veins at the edges of the plaquelike lesions; so I think this woman has perivasculitis, the cause of which is unknown.

Scabies. Presented by DR. JACK WOLF.

R. D., a woman aged 22, was first examined at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 7, 1942. She presented a pruritic eruption on the upper extremities, the sides of the chest and the neck of two months' duration. The lesions on the dorsal aspects of the hands, the forearms and the arms consisted of sharply defined pinhead-sized to bean-sized vesicular and crusted lesions resembling nummular eczema. The eruption on the sides of the chest was profuse and consisted of small crusted papules; on the neck the lesions were few and were scaly rather than vesicular. There were no lesions on the buttocks, along the belt line, in the axillary folds or around the mamillae.

The diagnosis of nummular eczema was entertained at the time, but because of a burrow in the web between the ring and the middle finger of the right hand scrapings of material were examined. Ova were found in the scrapings. Further studies demonstrated the acarus in scrapings from a nummular vesicular patch. Dr. Max Scheer had previously made the clinical diagnosis of scabies.

DISCUSSION

DR. MAX SCHEER: I saw the patient in the clinic, and the clinical diagnosis was confirmed by the finding of acari and ova in the nummular lesions on the forearm.

DR. E. WILLIAM ABRAMOWITZ: The unusual feature, of course, is the peculiar eczematous eruption. This could have been produced by rubbing of the lesions with medicaments.

DR. HERMAN SHARLIT: I am wondering whether this unusual reaction could be due to the fact that this patient may be sensitized to the organism, giving this unusual clinical picture.

DR. PAUL E. BECHET: I carefully examined the patient at the clinic and noted the same clinical picture she presents tonight, namely, circinate, sharply defined, vesiculobullous lesions, some of which exhibited erythematous halos. No scratch marks could be discerned. Between the webs of one or two of the fingers small bullae were noted. Despite the finding of acari, I still believe that the patient has a toxic bullous erythema. In my opinion there is no reason why a person with scabies cannot have concurrently as common a disease as erythema multiforme.

DR. MAURICE J. COSTELLO: I do not think it is unusual to see a patient with scabies and generalized urticaria due to sensitization to the itch mite, and I do not see why such lesions cannot become eczematized.

DR. DAVID BLOOM: I agree with Dr. Costello that such eczematous lesions are not infrequently met with in association with scabies. The fact that this patient has a seborrheic type of skin may also be a factor in production of the eczematous lesions.

DR. M. B. PAROUNAGIAN: I agree with the diagnosis. I think that the lesions are modified by the treatment received. One unusual feature is the absence of lesions around the nipple. Dr. Scheer deserves commendation for making this diagnosis.

DR. J. FRANK FRASER: Dr. Scheer's demonstration of the itch mite has clearly established the presenter's diagnosis.

DR. GEORGE M. LEWIS: The diagnosis of scabies has been proved. Nevertheless from a clinical standpoint there is also an eczematous rash of the type typical of parasitic or nummular eczema on various parts of the body. I believe the patient has both nummular eczema and scabies. I see no evidence of dermatitis from treatment. Another unusual feature is that when an orbicular lesion was scraped the itch mite was found. I believe that to be a unique observation. One might speculate whether the skin is less resistant in the areas of orbicular eczema. In any case it should be emphasized that the eczematous eruption in this patient is not of the clinical variety so often seen as a complication of scabies, either following trauma or occurring as a reaction to treatment.

DR. JACK WOLF: The parasite was demonstrated in a nummular lesion. That excludes the possibility of two different dermatoses. The explanation for the nummular eczematous lesions probably lies in the constitutional background of this patient. I think she has had latent eczema and the presence of the itch mite in her skin is sufficient to produce a nummular eczematous type of lesion.

Dermatitis Venenata (Etiology?). Presented by DR. E. WILLIAM ABRAMOWITZ.

M. F., a white man aged 26, American born of Jewish parents, married, was employed as a draftsman in an airplane factory. The eruption started three months ago on the outer side of his arms and spread to the rest of his arms and body, including the face. The feet were entirely clear. When he first appeared the eruption was most pronounced on his ear lobes, in the biceps area and on the shins. The rest of the body showed patches of diffuse erythema and scaling. The glans penis was involved. He was admitted to the New York Post-Graduate Medical School and Hospital.

While in the hospital, he showed a slight anemia, with 13 per cent eosinophils. The rest of the blood count showed no abnormalities. He was given patch tests with drafting paper and plain paper used in the plant where he works. He was also tested with shirts, wash cloths, lipstick, a deodorant and his wife's face powder. He had a slightly positive reaction to plain and to vellum paper. The patient

suspected laundered shirts, underwear and colored pajamas, but all these clues were followed up with no results.

The patient left the hospital slightly improved. He has had several relapses, one of which was attributed to wearing a woolen coat which had been packed in camphor and tar paper. A more recent attack was attributed to the use of a colored magazine. He had roentgen treatment with no relief. There was some improvement at times under bland therapy.

The reason for presentation is to obtain an opinion as to diagnosis and suggestions for further investigation and other clues as to the cause of this dermatitis. The patient refuses at present to have any further patch tests.

DISCUSSION

Dr. Isadore Rosen: It would be difficult to establish a diagnosis from one cursory examination. From the history, the present condition is different from some of the other phases through which this patient has passed. I therefore believe that the character of the lesions changes. This would fit in with the diagnosis of chronic lichenoid and discoid dermatitis. Unfortunately, while histologic examination may rule out other conditions, the histologic picture is not characteristic of this disease. The obstinacy to therapy and the recurrent attacks especially after the patient has been away from his occupation speak in favor of the suggested diagnosis.

Dr. George M. Lewis: I favor the diagnosis of Rosen's disease (lichenoid, discoid, exudative dermatosis). The diagnosis is difficult to make at this time because of the short duration, but there are a few lichenoid areas. The distribution of the eruption can hardly be explained on the basis of the contacts of this patient, and I doubt if the allergic study will help. The lesions on the penis, the intense itching, the race of the patient and the chronicity of the disease all point to the diagnosis of Rosen's disease.

Dr. Jack Wolf: I too favor the diagnosis of constitutional eczema as against eczema due to contact. Patients with this condition have gone to San Antonio, Texas, and other places and their eruptions have cleared up almost immediately, only to recur when the patients go back to New York.

Dr. Wilbert Sachs: While there are stages in which it may be difficult to differentiate microscopically between dermatitis venenata and chronic lichenified and discoid dermatitis, in other phases of these dermatoses it can be done. The location of the inflammatory reaction, the epidermic changes and the cellular infiltration are different in these diseases. While the cellular infiltration is of the simple variety in dermatitis venenata, in well established lesions of chronic lichenoid and discoid dermatitis plasma and even epithelioid cells may be found.

Dr. Herman Sharlit: I am satisfied that this patient's condition falls into the category of chronic lichenoid and discoid eruptions, now so frequently seen. I am somewhat chagrined that there is no surer feeling than I hear expressed tonight that all such conditions are initiated by dermatitis venenata. I have carefully studied 3 cases of this kind and was impressed with the importance of dermatitis venenata as a background.

Dr. Fred Wise: I am in agreement with Dr. Rosen's diagnosis of chronic lichenoid discoid exudative dermatitis. In the great majority of cases of this kind which I have had under personal observation, the history of a contact dermatitis in the beginning of the eruption has been obtained after careful history taking. Nevertheless, patch tests give negative results, as Sulzberger and his collaborators have stressed. A patient treated by Dr. Bechet and later by several other dermatologists had an eruption which at one time closely simulated mycosis fungoides, but the patient recovered after a long course of treatment of various kinds.

Dr. E. William Abramowitz: The patient presents a decided improvement since I started to treat him. The lesions are now dry and follicular with the exception of those on the shins and glans penis, which still show a mild weeping

dermatitis. I admit the eruption, as seen tonight, closely resembles the lichenoid discoid exudative dermatitis described by Drs. Rosen, Sulzberger and Garb. Besides the special clinical features presented by this dermatosis, the point is stressed that it is difficult to demonstrate any agent responsible for the eruption. To my mind this does not exclude that it is still possible for such a factor to exist. Therefore I am the "lone wolf" in still believing that this patient has dermatitis venenata. I have observed other instances, called cases of chronic lichenified eczema before they were labeled by a new term by Drs. Rosen, Sulzberger and Garb, in which the eruption subsided, and I always suspected that some contact agent or inhalant was responsible even though it could not be definitely proved. In this particular case, I suspect an overcoat which the patient has been wearing. It had been packed in camphor and tar paper for about five years before it was worn. I also suspect a colored illustrated technical magazine which the patient reads very often. The patient has not permitted any cutaneous tests to be made, and his skin has not been well enough. He has been using nothing but soothing remedies.

Lichen Planus and Fixed Drug Eruption? Presented by DR. ISADORE ROSEN.

W. B., a Negro aged 35, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 13, 1942 with an eruption of one year's duration on the forehead, at the right angle of the mouth, on the back of the neck, on the tongue and on the glans penis. Some of the lesions have been present only two months.

The patient presents on the forehead a dime-sized slate blue lesion. There are similar smaller lesions at the right commissure of the mouth and on the back of the neck. The tongue presents numerous bluish white papules. The whitish plaques seen on the buccal mucosa are of unknown duration.

The patient has been under antisyphilitic treatment by a private physician since the fall of 1939 (intravenous and intramuscular injections). The eruption on the face started after antisyphilitic treatment was begun. Since 1941 he has been receiving regular treatment for syphilis.

DISCUSSION

DR. JACK WOLF: I favor the diagnosis of lichen planus.

DR. E. WILLIAM ABRAMOWITZ: Even if that lesion on the forehead were lichen planus, if it flared up after the administration of mapharsen it would still be a fixed eruption. I believe it is the pigmented type of fixed drug eruption.

DR. GEORGE M. LEWIS: I favor the diagnosis of lichen planus.

DR. DAVID BLOOM: In my experience, I have found that lichen planus in Negroes is associated with excessive hyperpigmentation. In this patient the lesions are slate blue and are most probably fixed lesions due to arsphenamine. Whether the lichen planus eruption of the oral mucosa is also due to arsphenamine I am unable to say.

DR. WILBERT SACHS: Clinically, I believe that this patient has a fixed drug eruption. Pathologically, the absence of a lichen planus type of reaction would rule out lichen planus.

DR. MAX SCHEER: I do not agree with Dr. Sachs. If there is a lichenoid eruption from arsenic there is likely to be a structure indistinguishable from lichen planus, but in the case of a fixed drug eruption, as this is called, there will not be a lichen planus structure. If there is a lichen planus structure in this pigmented lesion it is lichen planus and not a fixed arsenical eruption.

Hidradenitis and Folliculitis. Presented by DR. JACK WOLF.

B. Z., a white man aged 23, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presents two related processes of

different duration. On the face, chest and shoulders he presents the remains of a previously active process of four years' duration in the form of pitted scars; the condition is most pronounced on the face. In the axillary, inguinal, pubic, crural and perianal regions he presents numerous smaller and larger pustular lesions. These are irregularly shaped, elevated, scarred lesions which are the result of recent active lesions now healing. There are also other open discharging lesions. This process has been present for the past six months.

The patient has been treated with various topical remedies and has received both filtered and unfiltered roentgen ray therapy as well as sulfathiazole (*2*-[paraaminobenzenesulfonamido]-thiazole) and sulfadiazine (*2*-[paraaminobenzenesulfonamido]-pyrimidine), without much benefit. Recent bacteriologic studies revealed diphtheroid organisms and nonhemolytic streptococci, and the patient is now being treated with a specific nonhemolytic streptococcus bacteriophage in aspargine medium.

DISCUSSION

Dr. Wilbert Sachs: I agree with the diagnosis but believe that there is something systemically wrong with this man. I should be especially interested in ruling out tuberculosis.

Dr. Anthony C. Cipollaro: I agree with the diagnosis, and I agree also that a thorough examination should be made, but I doubt whether anything will be discovered. I had the opportunity to study many similar cases when I was working with bacteriophage, and I seldom found any systemic disorders. Bacteriophage was found to be of little value in the treatment of this type of patient. The problem is a dermatologic one and requires therapeutic resourcefulness. I should use local antiseptic preparations, prolonged and frequent baths with potassium permanganate, generalized ultraviolet irradiation, vitamins, suitable diet, thyroid, sulfonamide compounds locally and systemically and if necessary roentgen rays. His environment may need to be changed.

Dr. E. William Abramowitz: Conditions that fail to respond to roentgen therapy become surgical problems.

Dr. George M. Lewis: In a recent case of this disease a complete investigation was totally devoid of any finding of value. I administered sulfathiazole with good temporary results.

Dr. David Bloom: In this case, as in cases of sycosis and of ulcerative pyoderma, the greatest attention is to be given to the general health of the patient. Although on general examination one usually does not find any definite abnormality, hygienic and supportive measures should be instituted to raise the general health of the patient. Regarding hidradenitis axillaris, I have never seen failure from roentgen treatment. About 1 erythema dose of roentgen rays filtered through 3 mm. of aluminum, given in fractional doses during a period of two weeks, will cure the condition. It is surprising to me to see physicians and surgeons trying to treat hidradenitis axillaris by surgical means, in many respects inferior to roentgen rays.

Dr. Maurice J. Costello: I agree with the suggestion of Drs. Lewis and Bloom that roentgen rays should be applied. At Bellevue Hospital the patients are given sulfathiazole tablets by mouth and a 5 to 10 per cent sulfathiazole cream or sulfathiazole powder is applied locally. I think that the results following oral and external administration of sulfathiazole are better than following the use of either one alone. If one judges from the good clinical results, it appears to make little difference what vehicle is used for sulfathiazole. If the eruption is amenable to treatment it will respond favorably. I have used it in equal parts of wool fat and petrolatum and at times with one of the new wetting agents. Sulfathiazole and not sodium sulfathiazole is used.

Dr. Paul E. Bechet: The patient presents the not uncommon picture of a severe type of acne conglobata, the course of which is similar to that of perifolliculitis capitis abscedens et suffodiens. This eruption of deep pustular,

indurated, multilocular abscesses with subsequent deep and disfiguring scarring invariably occurs in pasty-faced emaciated "run down" persons. Local treatment alone is valueless. To obtain a cure, which is possible, the treatment must be general as well as local. Iron and arsenic, vitamin therapy, generalized ultraviolet irradiation, rest outdoors and above all a total change of climate, in addition to the local treatment, are in my opinion the most important weapons in the therapeutic armamentarium against this disease.

Dr. M. B. Parounagian: I think stannoxyl (a preparation of metallic tin and its oxide) shows unusual results in such cases as this.

Dr. Fred Wise: My experience in cases of this kind is the same as that of Dr. Cipollaro. For eruptions which are not too far advanced and of relatively short duration, roentgen ray treatment combined with mild antiseptic applications usually produces excellent results. Surgical intervention is necessary only in cases of severe, deep-seated and distinctive forms of the disease, usually encountered in the axillary and inguinal regions.

Dr. Jack Wolf: This condition was so extensive around the genitalia and perianal region that I thought it was worth while showing tonight. The patient has come under my observation so recently that I have not had the opportunity of investigating him fully or of instituting any therapeutic regimen.

Mycosis Fungoides. Presented by Dr. Maurice J. Costello.

J. M., a man aged 57, is presented from the outpatient department of St. Clare's Hospital.

He presents a lesion on the left side of the face and right side of the scalp of eight months' duration and a lesion on the deltoid region of the left arm which has been present for one year. The lesions are plaquelike, showing various degrees of infiltration in the individual lesions and in the eruption generally.

The Wassermann reaction of the blood was negative.

DISCUSSION

Dr. J. Frank Fraser: I had the opportunity within the last fortnight of observing a straightforward case of mycosis fungoides with lesions in all stages of development, ranging from noninfiltrated scaly areas and palpable infiltrated plaques to fungoid tumors. The histologic picture in a section taken from a raised lesion was that of reticulum cell lymphosarcoma. The gross appearance in many of the lesions was identical to that seen in Dr. Costello's case. There was no appreciable involvement of the lymph nodes, and there is no evidence of lymphadenopathy in the case under discussion. One must be on guard against making the mistake of laying too much stress on the feature of adenopathy in mycosis fungoides. Lymphadenopathy is secondary and often a late feature of this disease. Mycosis fungoides arises in the perivascular reticulum cells of the skin. It is a primary disease of the skin. While I agree with the presenter's interpretation, the diagnosis should not be recorded as final without microscopic confirmation.

Dr. David Bloom: I should consider two diseases, tuberculosis and syphilis. I should favor the diagnosis of tuberculosis in spite of the comparatively short period (one year) during which the lesion developed. However, a final diagnosis must be entrusted to the microscopic study.

Dr. Wilbert Sachs: I believe that this patient has mycosis fungoides.

Dr. Herman Sharlit: My first guess would be against mycosis fungoides, but if the disease is mycosis fungoides I could understand it. If the histologic examination fails to reveal that diagnosis, in spite of the negative Wassermann reaction I should be inclined to treat this patient for syphilis.

Dr. Isadore Rosen: The impression that I got from the clinical examination was some form of granuloma but not mycosis fungoides. The features closely resemble some form of syphilis or tuberculosis. Despite the fact that the patient

has a negative Wassermann reaction, I suggest that he be given a bismuth compound intramuscularly and potassium iodide by mouth.

DR. ANTHONY C. CIPOLLARO: This is the type of condition that I think is difficult to diagnose without a biopsy. My first clinical impression was that of lupus vulgaris tumidus. There are also features of mycosis fungoides.

DR. E. WILLIAM ABRAMOWITZ: This case puzzles me. I am reminded of several cases in which the differential diagnosis was between mycosis fungoides, syphilis, tuberculosis and deep ringworm infection. The disease finally turned out to be pyoderma. This diagnosis has to be considered in this case.

DR. GEORGE M. LEWIS: In spite of the lack of itching the configuration suggests mycosis fungoides, but it is difficult to differentiate the disease from tuberculosis and syphilis. Besides the biopsy, it would be instructive to administer to one of the lesions a mild dose of roentgen rays.

DR. M. B. PAROUNAGIAN: I do not believe that the patient has either syphilis or mycosis fungoides. I think Dr. Bloom's suggestion of tuberculosis is more likely than anything else.

DR. MAURICE J. COSTELLO: I think it would be unusual for lupus vulgaris to occur in three areas almost simultaneously and be of only one year's duration in a person of his age. He has had a moderate degree of itching. The Wassermann reaction of the blood was negative.

NEW YORK DERMATOLOGICAL SOCIETY

J. GARDNER HOPKINS, M.D., *President*

A. BENSON CANNON, M.D., *Secretary*

March 24, 1942

Keratosis Plantaris. Presented by DR. PAUL E. BECHET.

G. L., a woman aged 26, from the New York Skin and Cancer Hospital, states that her lesions began when she was 14 and have progressively enlarged and thickened since that time. Her father has diabetes, and her maternal grandmother also had diabetes. Both her father and mother have callosities but are not inconvenienced by them.

The results of the patient's dextrose tolerance tests were normal. Between 1935 and 1938 she received twenty roentgen treatments of undetermined dosage at another institution. A few months after her last treatment a necrotic area developed on each heel, which healed after six months but which have recurred off and on since then.

On inspection both soles exhibit large raised dark gray, horny masses from 1 to 1.5 cm. thick. One of them extends from the distal phalanx of the great toe, across the sole at right angles, ending at the middle of the metatarsal arch, describing an L-shaped course. The masses are sharply outlined, and the adjacent skin is normal.

In January 1942 the keratosis on the left heel was removed and replaced by a full thickness Thiersch graft taken from the buttock. This graft took except for a silver dollar-sized area, which is ulcerating.

A histologic diagnosis of keratosis was made by Dr. Charles F. Sims.

The patient is exhibited because of the unusual severity of the lesions and for therapeutic suggestions.

DISCUSSION

DR. GEORGE C. ANDREWS: I agree with the diagnosis as presented. The problem of treatment is difficult. After excision of the lesions, even if the graft

takes successfully—as this one did not—keratotic warty lesions are likely to develop alongside the graft or even in the graft. I have had a patient under my care for twelve years. She came to the hospital as a child of 8 years with lesions almost identical with this patient's. They were excised several times by a plastic surgeon, but they recurred. The grafts were of full thickness. It is difficult to explain how the lesions can recur, but they did and the plastic surgeons have given up trying to excise them. Roentgen rays and radium are of course of no benefit.

DR. EUGENE F. TRAUB: In view of the definite evidence of radiodermatitis about some of the lesions and because of Dr. Andrews' remark that the keratoses might possibly recur after skin grafting, I should replace the affected area with scar tissue by removing the lesion with the electric cutting current. The defect must then be permitted to granulate in from the base and sides, the area being replaced with a scar, in which the keratoses are less likely to recur. The only question in this case is the amount of irradiation damage that has been done and how well the wound would heal after such a procedure.

DR. GEORGE M. MACKEE: All of the patients with this disease that I have seen have had diabetes or incipient diabetes or have become diabetic later, and they often give a history of familial diabetes. I have not found any satisfactory treatment for these lesions. They are likely to recur, even in scar tissue, as has been stated. My best results have been with palliative treatment. I recommend soaking the feet in some hot solution for a long while to soften the horny layer; then this layer is pared level with the normal skin with a razor blade, and the lesion is treated with a salicylic acid plaster or a strong salicylic acid ointment, as strong as 50 per cent. Such treatment does not cure, but it often permits vocational or avocational activities in comfort. At times it is possible to adjust pads so as to remove pressure from the lesion, which also often is of benefit.

DR. JEROME KINGSBURY: I agree with Dr. Traub that it would be preferable to go deeper and have the lesions replaced by scar tissue rather than to attempt a graft. The prognosis for a lasting result is not good.

DR. A. BENSON CANNON: I feel much as Dr. MacKee does, that palliative treatment is more beneficial in keratosis plantaris than is radical removal of the affected parts. I usually employ a 60 per cent salicylic acid dressing and trim the thickened tissue to the level, or slightly below, of the surrounding skin and have the patient wear a protective plaster or pad. The present case is complicated by an area of radiodermatitis in the center of which is a cutaneous hornlike growth that must be considered as a probable beginning epithelioma. I therefore suggest complete destruction of the horny growth and atrophic and telangiectatic areas with electrocoagulation. Plastic surgery could be used later if necessary.

DR. GEORGE C. ANDREWS: Since Dr. Cannon mentioned squamous cell epithelioma, I should like to report on a case I observed several years ago, in which I advised excision but the surgeons there did not want to excise the lesion and used salicylic acid instead. A squamous cell epithelioma developed and the patient died. I attributed the death to the salicylic acid treatment. Also, as far as recurrence in scar tissue is concerned, these keratotic lesions will recur even in sclerotic tissue following radiodermatitis.

DR. A. BENSON CANNON: Palliative treatment of the lesions on the heels would not be indicated in this particular case because of the radiodermatitis.

DR. PAUL E. BECHET: The patient has received all of the treatments suggested in the discussion. Whether these therapeutic measures were adequately employed I do not know.

Scleroderma (Generalized, Progressive Type). Presented by DR. FRED WISE.

L. M., a woman aged 66, registered at the New York Skin and Cancer Hospital on April 28, 1936, presenting a dermatitis on the trunk and sides of the neck

(sulfur?) of several weeks' duration. She was a hairdresser and came in contact with dyes and chemicals. Examination at that time showed that the skin was dry, wrinkled, slightly scaly and pigmented from light to dark brown. She complains that for the past seventeen years her left leg has been "going to sleep"; this condition is relieved by walking.

The present eruption dates back to October 1941. It began with itching on the thighs, which then spread to different parts of the body. About a month later the patient began to feel a tightness in both thighs and shortly after that similar sensations in the breasts. The areas of tightness corresponded with the areas of itching. At about the same time she also noticed a discoloration of the skin. The patient thinks that some areas have become softer. During this period she has lost "a lot of hair" and 7 pounds (3.2 Kg.) in weight. The family history is irrelevant.

Almost the entire cutaneous surface of the face is yellowish or carotenoid in color. The breasts are uniformly silvery white and feel taut, and the areolas and the nipples are the only parts not affected. There are telangiectatic capillaries on the entire upper aspect of the chest. On the greater portion of the abdomen are diffuse areas of scleroderma of yellowish brown. There is a similar but less infiltrated area extending from the mid-dorsal region to the end of the coccyx; this is 13 cm. in its widest diameter. There are fairly well defined symmetric areas involving almost the entire upper and inner surfaces of the thighs. Continuous sclerodermatous linear areas extend from the patellas to the dorsal surfaces of the feet. The scalp shows diffuse alopecia. The hair is thin and dry. Protruding from the hard palate and adherent to it is an irregular hard reddish growth about 5 cm. in length, 1 cm. in width and 0.5 cm. in thickness. The surface is smooth and covered with telangiectatic capillaries. The teeth are in poor condition.

The results of routine laboratory tests were normal except for an erythrocyte count of 3,790,000, of which 8 per cent were polymorphonuclear eosinophils. The results of chemical examination of the blood on March 5, 1942 were as follows: urea nitrogen (normal 10 to 15 mg.) 20 mg. and nonprotein nitrogen (normal 25 to 35 mg.) 42 mg. per hundred cubic centimeters of whole blood, with a ratio (normal 35:45) of 47 per cent; inorganic phosphate (normal for adults 3.5 to 4.0 mg.) 4.5 mg. per hundred cubic centimeters of serum; chlorides and true dextrose in the blood and calcium in the serum, normal; total cholesterol (normal 160 to 230 mg.) 260 mg. and esters (normal 100 to 150 mg.) 155 mg. per hundred cubic centimeters of serum, with a ratio of esters to total cholesterol (normal 40:60) of 59 per cent. A urea clearance test, corrected for surface area, showed a renal function of 62 per cent of the average normal in the first hour and 89 per cent in the second hour (normal 75 to 150 per cent). Vitamin C in the blood plasma was normal, 0.9 mg. (normal 0.7 to 1.4 mg.) per hundred cubic centimeters. The vitamin C saturation test (urinary excretion after injection of 1 Gm. of ascorbic acid intravenously) gave a normal saturation index of 575 mg. in twenty-four hours (normal over 500 mg.). Urinary androgen studies showed 13.5 mg. of 17-keto steroids in twenty-four hours in 2,430 cc. of urine voided (normal for females 9 to 20, average 16 [New York Post-Graduate Hospital figures]).

Vascular investigation by Dr. Strauss disclosed that the "oscillometric readings were within normal limits. The plantar ischemia was negative and Allen test normal." Otolaryngologic examination showed that the septum was hypertrophic, deviated to the left, and the middle turbinates enlarged. Ophthalmoscopic examination showed normal disks and maculas and some sclerosis of the lenses. A roentgenogram of the thorax revealed a relatively large heart and considerable calcification in the hilar lymph nodes, with secondary central thickening mainly toward the bases of the lungs. The basal metabolic rate was normal. The electroencephalographic report (Dr. Bernard L. Pacella) disclosed that "diffuse abnormal electrocortical activity of only a moderate degree appears to be present. There is no indication of a localized lesion. The character of this pattern has

often been noted in patients presenting some diffuse chronic degenerative condition of the cortex or in patients with lowered activity of the cortex."

A specimen removed from the left thigh and examined histologically by Dr. Charles F. Sims showed the changes of scleroderma. The epidermis was flattened throughout most of the section. The rete pegs and papillary bodies were for the most part obliterated. The cutis presented a condensation of collagen bundles most manifest in the upper part and midportion, arranged more or less parallel to the surface. No hair follicles were visible. The vessels were considerably compressed, many of them completely obliterated. In scattered parts of the section one could note an occasional dilated lymph vessel. The elastic tissue was unaffected.

The patient has been treated since March 19, 1942 with subcutaneous injections of prostigmine methylsulfate, 1:2,000, 1 cc. each, three times weekly. She is taking orally prostigmine bromide, one tablet (15 mg.) three times a day. She has also been advised to massage the lesions frequently with cocoa butter.

DISCUSSION

DR. A. BENSON CANNON: The unusual location and the yellow color of the sclerodermatous skin are most interesting.

DR. GEORGE M. MACKEE: I think the case is one of scleroderma, both clinically and histologically. I refer to the skin, not to the oral lesion.

DR. EUGENE F. TRAUB: I agree with the diagnosis but believe that the lesion on the hard palate is a torus palatinus rather than part of the picture of scleroderma.

DR. J. FRANK FRASER: If I had not seen the gross lesions, I should have made the diagnosis of scleroderma from the histologic picture. It is typical.

DR. HOWARD FOX: I think that in discussing cases of localized scleroderma, either "scleroderma" or "morphea" should be used to explain what is meant. The lesion on the thigh seemed to be a classic patch of localized scleroderma. I do not think the lesion on the palate has anything to do with this disease.

Erythema Multiforme Bullosum Complicating Pregnancy (Herpes Gestationis?). Presented by DR. A. BENSON CANNON.

Mrs. A. E., a white woman aged 23, an American housewife, was admitted to New York City Hospital, Welfare Island, on March 6, 1942, with a generalized bullous erythematous eruption accompanied by intense itching and burning which had persisted since the middle of June 1941, when she was three months pregnant. It began with bullae on the palms and soles, which gradually became generalized. She was admitted to a local hospital and was later transferred to the Woman's Hospital, where she remained until three months after the birth of her child. She had been confined to a hospital with the same type of eruption in December 1938. It had appeared when she was seven months pregnant and led to a premature birth and the death of the child. The skin gradually cleared six weeks after the miscarriage, and she remained well until the present attack.

When I first saw the patient at the Woman's Hospital she had almost universal involvement of the skin with great swelling of the extremities. The eruption consisted mostly of flaccid bullae filled with thin yellowish material. Some bullae had ruptured, leaving raw surfaces. On the other parts of the skin there were urticarial and erythema multiforme types of lesions. The patient was ill, having a temperature of 100 to 103 F. She had a leukocyte count of 15,000, with 82 per cent polymorphonuclear leukocytes. Another leukocyte count was 29,200, with 59 per cent polymorphonuclear cells, 29 per cent eosinophils, 10 per cent lymphocytes and 2 per cent monocytes. Cultures of the bullae showed only staphylococci.

The patient was given sodium bicarbonate baths twice daily and boric acid ointment dressings on the extremities, milk of bismuth on the trunk, sodium thiosulfate intravenously and orally and sodium citrate and generalized ultraviolet irradiation with a carbon arc lamp. She improved greatly and became normal.

The swelling disappeared, and while there remained some urticarial and erythema multiforme-like lesions, she was sufficiently well to be discharged from the hospital after six weeks. She was at home only two weeks and was readmitted because of acute edema of the extremities and multiple bullae. She remained in the hospital until she gave birth to a healthy boy, at full term, with a normal delivery. At birth the baby also had lesions of erythema multiforme; they were generalized, being more pronounced on the forehead and the front of the body. The condition of the mother grew worse after parturition, and her treatment was then changed to potassium permanganate baths and applications of calamine liniment locally and injections of adrenal cortex extract. Although the local infection disappeared and the swelling cleared, she did not improve otherwise. Therefore, she was transferred to the New York City Hospital. Her improvement has been rapid since admission, with only applications of boric acid ointment locally, sodium bicarbonate baths and injections of whole blood and of adrenal cortex extract. The results of a complete physical and neurologic examination and of all laboratory tests were essentially normal. The only positive finding has been Staphylococcus aureus, cultured from both the clear and the cloudy bullae. A roentgenogram of the chest and roentgenograms of the gastrointestinal tract and gallbladder were all normal. Chemical examination of the blood showed 25 mg. of nonprotein

Erythema multiforme bullosum complicating pregnancy.

nitrogen and 90 mg. of sugar per hundred cubic centimeters. The Wassermann reaction of the blood was negative. The result of a sedimentation test was reported as 38. The blood platelet count was normal. The erythrocyte count was 4,800,000, with 84 per cent hemoglobin.

DISCUSSION

DR. GEORGE M. MACKEE: I have a patient in the hospital now who is four months pregnant and has a similar condition of three months' duration. The diagnosis in such cases is important but difficult. One must think of erythema toxicum or erythema multiforme bullosum due to pregnancy, herpes gestationis (possible variant of Duhring's disease) and impetigo herpetiformis (often fatal). In my case I made three biopsies, taking one specimen from an early vesiculopustule with surrounding erythema, one from a lesion that had progressed to the size of a dime and the third from a lesion that had undergone some regression. There is nothing in the histologic picture except what can be called a toxic dermatitis. The bulla is between the granular layer and the horny layer, as in impetigo. Until recently there has been no grouping, but lately there has been a tendency for new lesions to occur in groups. The elementary lesion is a vesicle, but there are also scaly, moist patches with some configuration, such as one sees in impetigo contagiosa. In places these lesions join to form a large sheet of eruption.

DR. EUGENE F. TRAUB: Was this the second time this condition occurred, and were there two babies who had this eruption?

DR. A. BENSON CANNON: The patient's first pregnancy ended in a miscarriage.

DR. EUGENE F. TRAUB: Is it correct that this eruption began this time before the baby was delivered and continued for some time after delivery?

DR. A. BENSON CANNON: Yes. The eruption began about two months after the patient became pregnant and continued for six weeks after delivery. The baby was born with erythema multiforme lesions on the forehead, cheeks and trunk.

DR. GEORGE C. ANDREWS: I was interested in the point as to how serious this eruption is. It is usually stated that such eruptions may have some serious portent. I have had 3 or 4 cases of this kind and have always worried that the outcome might be serious. The obstetricians have looked for various causative factors, but the patients have gone along with normal pregnancies and had no serious outcome. I have a case in mind in which I experimentally treated one arm and leg with roentgen rays and did not treat the other arm and leg. The lesions treated with roentgen rays healed more quickly, which is of some interest. I saw a patient this morning with a similar condition, a bullous erythema multiforme, which she has had for eighteen months. It appeared two days after the delivery of her last baby. She had never had it before. The eruption has been present on the face, legs and forearms ever since. She has had a high leukocytosis at times, up to 20,000. Nothing had done her any good until I gave her some acetarsone. The eruption cleared up for the first time in eighteen months. She took the drug for eight days. She came in today and the eruption is gone. I think arsenic is of value in these conditions.

DR. HOWARD FOX: In view of Dr. Andrews' statement about the prognosis in such cases, I think the society should go on record in this matter. As far as I know, this condition is almost invariably benign. It disappears either at the time of parturition or shortly afterward.

DR. A. BENSON CANNON: Two specimens for biopsy were taken, one from an erythema multiforme lesion and the other from a bulla. In both instances the histologic diagnosis was erythema multiforme, no mention being made of the location of the bullae. The patient's eruption has been complicated by severe constitutional symptoms suggestive of a profound toxemia, which could not be explained by the infected bullae. She has also had leukocytosis and a high sedimentation rate. The obstetricians gave a bad prognosis both for the outcome of the pregnancy and also for the life of the mother. Of the number of cases of herpes gestationis and erythema multiforme that I have encountered over a period of more than twenty years, I have never seen a fatal termination. In fact, most of the patients have not been seriously ill. This patient has had arsenic in the form of both arsphenamine and acetarsone. No improvement followed the use of either drug.

DR. GEORGE M. MACKEE: Apropos of the statement Dr. Fox made, I repeat that the diagnosis is important in these cases. Dr. Cannon's patient had a polymorphous eruption with erythematous plaques, urticarial wheals and bullous lesions. My patient has a similar multiforme eruption. Therefore, in both cases the diagnosis is erythema multiforme occurring in pregnancy, a benign disease. Impetigo herpetiformis is rare and, as the name implies, there are groups of vesicles. This disease is apt to prove fatal unless pregnancy is interrupted.

DR. EUGENE F. TRAUB: How many times is a bullous erythema multiforme present on the baby?

DR. GEORGE M. MACKEE: A bullous eruption occurring on the baby is uncommon, but it does occur.

DR. EUGENE F. TRAUB: Would that not be suggestive of a drug eruption? Dr. Cannon has said that he attempted to exclude the possibility. Is he absolutely sure?

DR. A. BENSON CANNON: I have ruled out a drug's being responsible for the erythema multiforme both in the mother and in the child. The patient had been confined to the hospital for a number of months, during which time no drugs had been administered. The examination of the blood for bromide gave negative results, and the urine showed no iodide.

Acrodermatitis Chronica Atrophicans with Juxta-Articular Nodes and Pseudoscleroderma. Presented by DR. PAUL E. BECHET.

B. G., a man aged 51, from the New York Skin and Cancer Hospital, shows many juxta-articular nodes extending from the extensor surface of the left elbow to the middle of the posterior surface of the forearm. They vary from 2 to 5 cm. in width and are 1.5 cm. in thickness. They are freely movable and painless. The skin over them is atrophic and adherent. There are similar but much smaller nodes on the right forearm and several large ones above both knees. On the knees, thighs and backs of the hands, the characteristic parchment-like, semitranslucent, reddish brown skin of typical acrodermatitis can be observed. On the lower halves of both legs there are scleroderma-like changes. The patient was first observed by the presenter at the clinic in 1936; at that time he presented the same clinical picture, but it was not nearly so extensive.

A histologic diagnosis of scleroderma and acrodermatitis was made by Dr. Satenstein. On the patient's return to the clinic, in March 1942, the results of all routine laboratory tests were found to be within normal limits.

DISCUSSION

DR. J. GARDNER HOPKINS: Are the subcutaneous fibroid nodules a part of the disease?

DR. FRED WISE: I agree with the diagnosis as presented. The fibrous nodules in the vicinity of the elbows are late manifestations of the disease and appear after the atrophic process has become manifest. The nodules are usually situated in the so-called ulnar band over the ulnar aspect of the forearm.

DR. J. GARDNER HOPKINS: These nodules were in areas where there had not been any atrophy.

DR. HOWARD FOX: I think this is a typical case except that it is a little unusual to see this disease in men. The varicose dermatitis which he also presents has nothing, of course, to do with the acrodermatitis.

DR. EUGENE F. TRAUB: I presented before the New York Academy of Medicine in November 1933 (ARCH. DERMAT. & SYPH. **29**:760 [May] 1934) a man who had been in the hospital for some time and who showed the same legions as does Dr. Bechet's patient. The nodular lesions on the elbows were not necessarily on the sites of previous atrophy but occurred on the elbows and fairly well down on the extensor surfaces of the forearms. Incidentally, I performed quite a large number of biopsies, and on one or two occasions the question arose as to whether the condition was a lymphoblastoma or mycosis fungoides.

DR. J. GARDNER HOPKINS: There may be no basic distinction between Herxheimer's acrodermatitis and scleroderma, but this patient's condition looks like scleroderma. The lesions on the lower parts of the legs are thickened and indurated, and there are no areas of paper-like atrophy that I could see except on the shins, where there were some secondary changes. The backs of the hands are eczematous.

DR. HOWARD FOX: He showed atrophy on the backs of the hands.

DR. EUGENE F. TRAUB: Yesterday I saw a patient with well advanced acrodermatitis chronica atrophicans and scleroderma. That is a common association, the two diseases occurring in different areas on the same patient.

DR. PAUL E. BECHET: This case is interesting because in 1936, when I first observed him, the juxta-articular nodules were much smaller than they are now. They have increased greatly in size since then. There is, of course, around the knees and on the thighs and hands, as Dr. Fox has pointed out, a rather typical acrodermatitis chronica atrophicans. The thickening on the legs may be due to varicosities, but, as Dr. Traub and Dr. Wise have demonstrated, there is also a scleroderma or pseudoscleroderma present. Acrodermatitis in men is rather rare, especially when associated with juxta-articular nodules, and I am presenting this case for that reason.

Cutaneous Manifestations in Hodgkin's Disease. Presented by DR. J. FRANK FRASER.

A. G. L., a man aged 65, was previously presented before the Manhattan Dermatologic Society on March 11, 1942 (ARCH. DERMAT. & SYPH. **46**:587 [Oct.] 1942).

DISCUSSION

DR. A. BENSON CANNON: The onset of this disease with glandular enlargement would indicate that the patient had either Hodgkin's disease or lymphosarcoma. The disappearance of the glands after radiotherapy would tend to confirm this suspicion, although I do not recall having seen cutaneous lesions similar to this patient's in instances of either of these diseases. The circinate, configurated outline with infiltration of the cutaneous lesions looks strikingly like those seen in mycosis fungoides or psoriasis. I think that the final diagnosis must be a pathologic one. I believe (from the section shown to me by Dr. Fraser) that the pathologic diagnosis is Hodgkin's disease.

DR. R. H. RULISON: As I understand it, there are two types of cutaneous lesions which occur in Hodgkin's disease, one being true Hodgkin's disease of the skin, in which the biopsy will show a positive diagnosis of the disease, and the other being a toxic manifestation, which can take almost any form. I am a little uncertain as to what the histologic picture showed in this case. Was it described as Hodgkin's disease of the skin?

DR. J. FRANK FRASER: Biopsy of a specimen of skin showed a nonspecific dermatitis.

DR. R. H. RULISON: I presume, then, that this patient has the second type, or a toxic eruption. My impression is that one cannot make a diagnosis of Hodgkin's disease from the toxic type of eruption.

DR. GEORGE M. MACKEE: I am not willing, on the evidence thus far submitted, to accept the diagnosis of Hodgkin's disease. The histologic examination of the gland shows a lymphoma. There is no polymorphism. It shows an infiltration of small lymphocytes with a number of mitoses. There are no Dorothy Reed cells. That picture can represent lymphosarcoma just as well as Hodgkin's disease. The histologic picture of the skin was that of a nonspecific dermatitis. When this patient was presented before the Manhattan Dermatologic Society, he showed a similar picture, and at that time I did not think mycosis fungoides could be ruled out on the evidence submitted, in spite of the glandular enlargement and the histologic structure of the glandular tissue. The disease may be a lymphoblastoma of some type and may eventuate in mycosis fungoides. The response to roentgen therapy and the configurations and slight infiltration of the plaques should at least make one suspect the prefungoid stage of mycosis fungoides.

DR. EUGENE F. TRAUB: In this type of case I have seen urticarial lesions and a bullous type of lesion. Dr. Wise will probably discuss this fully, as he showed me a picture of a patient with Hodgkin's disease who had urticarial lesions and also annular and configurate lesions such as this patient presented. Therefore I presume it is possible to see almost any type of cutaneous eruption in cases of the lymphoblastomas, but since Dr. Fraser has not proved it in this particular case, it can only be an assumption at this time.

DR. HOWARD FOX: If this patient has Hodgkin's disease, I think the generalized eruption on the trunk is of the so-called toxic type. It is certainly not the lymphogranulomatous type of Hodgkin's disease either histologically or clinically. I agree that this is a most unusual type of eruption to be seen in connection with Hodgkin's disease, which is usually urticarial or prurigo-like. In this case it consists of circinate or solid plaques suggesting ringworm. I agree with Dr. Traub that this patient may conceivably have a toxic eruption of Hodgkin's disease, though the burden of proof is on the one who makes this diagnosis.

DR. FRED WISE: My impression is the same as that of Dr. Traub.

DR. GEORGE C. ANDREWS: There have been many cases of Hodgkin's disease reported in which mycosis fungoides has later developed, and this may be one of them, although the histologic structure of the cutaneous lesions from Dr. Fraser's description is not at all suggestive of mycosis fungoides. It is more suggestive of a toxic eruption occurring in lymphoblastoma. Since the two diseases are so closely related in every way, it is logical to suspect that in some rare instances one may see the same toxic eruption in Hodgkin's disease that occurs in leukemia. I have never seen such an eruption in Hodgkin's disease before. Most eruptions in Hodgkin's disease are similar to erythema multiforme or pruriginous or bullous, although I agree that this type may conceivably occur.

DR. J. GARDNER HOPKINS: If I recall correctly, Dr. Fraser's first diagnosis of the histologic section was lymphosarcoma. Others also thought it was lymphosarcoma. Will Dr. Fraser in closing the discussion tell how he arrived at the diagnosis of Hodgkin's disease?

DR. J. FRANK FRASER: In answer to Dr. Hopkins' question, it is true that my interpretation of the histologic picture was lymphosarcoma, but there was a difference of opinion among others who examined the sections, and a final microscopic diagnosis was not agreed on (see history). The diagnosis of Hodgkin's disease was arrived at by a consideration of the symptoms and clinical course of the disease. Cutaneous manifestations like these are rarely if ever seen in lymphosarcoma. The history of intense generalized pruritus is one of the chief cutaneous manifestations which either precedes or accompanies Hodgkin's disease. Replying to those members who entertained the diagnosis of mycosis fungoides, while it is true that the cutaneous lesions in this case bear a strong resemblance to those of mycosis fungoides and that intense pruritus is also a feature of mycosis fungoides, the diagnosis of mycosis fungoides can be excluded. Mycosis fungoides is a disease of the skin from the beginning. The initial lesion is always in the skin, never in the lymph nodes; involvement of lymph nodes is always secondary. In the case under discussion the initial lesion was in the cervical lymph nodes and the cutaneous manifestations did not appear until three years later. For these reasons the diagnosis of mycosis fungoides may be excluded.

Solid Edema of the Face. Presented by DR. HOWARD FOX.

A. S., aged 55, an Italian-American, is an employee of the Department of Sanitation. His work consists of draining swamp lands. He has no indigestion and drinks alcohol sparingly.

The eruption appeared two years ago and is situated on the middle two thirds of the face, including the forehead, nose, eyelids and cheeks. It consists of a symmetric, diffuse area which is bright red and warm to the touch and shows slight branny scaling. There is a moderate amount of edema, which is most noticeable on the eyelids and which does not pit on pressure. The severity of the edema varies at different times, being worse in damp or rainy weather. At times the eyes are completely closed. The general health is good. Examination of the eyes, nose and throat showed no abnormalities.

DISCUSSION

DR. A. BENSON CANNON: I agree with the diagnosis of solid edema of the face. I suggest the use of sulfanilamide.

DR. EUGENE F. TRAUB: I do not believe that any type of therapy will influence these lesions in the slightest degree. I believe they will be permanent.

DR. FRED WISE: What makes Dr. Traub so pessimistic? Does not roentgen treatment help this disease? I suggest a thorough trial of intravenous injections of bacteriophage, administering it every other day for ten or twelve injections.

DR. GEORGE C. ANDREWS: I am not as pessimistic as Dr. Traub. As Dr. Wise has suggested, I think roentgen treatment might help this man. It might not cure him, but it might help or improve the condition to some degree. I suggest the use of sulfadiazine nose drops every night. Also, cultures might be made of the nasal secretions and a vaccine made from these secretions.

DR. J. GARDNER HOPKINS: One usually thinks of solid edema of the face as being the result of chronic erysipelatous attacks. The areas of edema are usually not very symmetric. They may be present on both sides of the face but do not match exactly, as in this man. This patient attributes his condition to exposure to the sun and weather in his work. I wonder if it can be due to that? If so, then cultures of the nasal secretion and desensitization to staphylococcus toxin and the other types of therapy used for infectious diseases would not help him at all. The edema is so perfectly symmetric that I wonder if it is infectious. Besides, there is no history of any acute or erysipelas-like attacks. I should like to ask the presenter if this man has had a blood count and whether he might possibly have leukemia?

DR. HOWARD FOX: It has been difficult to get a history from this patient. Although he says he has had exacerbations at times with complete closure of the eyelids, I could not get a history of anything that suggested an erysipelatous attack. I do not agree with Dr. Hopkins that conditions of this kind are nonsymmetric. Whether the process is infectious or not I do not know. There is a tendency for physicians to assume that such a condition is due to a low grade streptococcic infection, and in past years vaccines made from the secretions of the nose have been used. Unlike Dr. Andrews, I have never had any success with them.

A Case for Diagnosis (Erythroplasia? Chronic Benign Familial Pemphigus?). Presented by DR. GEORGE M. MACKEE.

F. R. S., a white man aged 70, a retired minister, was previously presented before the Manhattan Dermatologic Society on March 11, 1942 (ARCH. DERMAT. & SYPH. **46**:592 [Oct.] 1942).

DISCUSSION

DR. A. BENSON CANNON: The history and the clinical appearance of the lesions are those of dermatitis vegetans. The red, granular, warty-like, ulcerated, half-dollar-sized area on the left side at the base of the penis suggests a beginning carcinoma. One must always bear in mind the possibility of epithelioma appearing as a result of long-standing irritation in an elderly person. I advocate complete removal by curettage followed by cauterization with trichoroacetic acid as a means of curing the disease. I have successfully treated several patients with similar lesions by the aforementioned method when all other remedies had failed.

DR. JEROME KINGSBURY: My impression is similar to Dr. Cannon's. I regard the case as one of infectious dermatitis vegetans. However, I am less optimistic about the prognosis and the effectiveness of the suggested therapy.

DR. PAUL E. BECHET: If one discounts the histologic report and depends entirely on the clinical appearance of the lesion, some interesting points are brought to light. The patch is large and exudative, with a sharply defined rolled edge at certain parts of its periphery. It has the angry red, moist, unhealthy granulation-tissue-like surface so often observed in epitheliomatosis. In addition, there are several nodules scattered through it. In view of these facts, a diagnosis of extramammary Paget's disease should be entertained. Extramammary Paget's disease has been reported by many different observers, among whom may be

mentioned Drake and Whitfield (*Brit. J. Dermat.* **41**:177, 1929), Busman and Woodburne (ARCH. DERMAT. & SYPH. **24**:396 [Sept.] 1931) and Weiner (*Am. J. Cancer* **31**:373, 1937), who found 57 cases in the literature and added 1, in which the condition was vulvar. In all of the cases reported the histologic picture of Paget's disease was noted. As early as 1904 and 1905 Fordyce and Fox (*J. Cutan. Dis.* **23**:193, 1905) and Fox and MacLeod (*Brit. J. Dermat.* **16**:41, 1904) reported the histologic changes of extramammary Paget's disease.

DR. EUGENE F. TRAUB: I agree with Dr. Bechet. The sharp border and the fact that parts of the lesion are dry and parts are moist, together with the growth that seems to be taking place at the base of the penis, show that the original process may now be undergoing secondary changes to epithelioma. The initial disease may well have been a Bowen tumor. I believe that Bowen's disease is one of the diagnoses that Dr. MacKee has considered under the heading of erythroplasia.

DR. J. FRANK FRASER: While there are changes in the epidermis suggestive of benign familial pemphigus, there is no familial history. I lean toward the diagnosis of erythroplasia. I also feel that malignant transformation is imminent, especially in those hard infiltered areas in the borders of the lesion. More biopsies should be made. In regard to the suggestion that this may be a case of "extramammary Paget's disease of the nipple," I wish to state emphatically that this term should never be used. There is no such disease as extramammary Paget's disease of the nipple. Paget's disease of the nipple is a cancer of the intraepidermal portions of the mammary ducts. The disease reported as extramammary Paget's disease was either Bowen's disease or cancer of the sweat or preputial glands (Fraser J. F.: ARCH. DERMAT. & SYPH. **18**:809 [Dec.] 1928).

DR. EDWARD R. MALONEY: While Dr. MacKee was reading the history of this case I thought he was giving a good description of dermatitis vegetans, in spite of the fact that the eruption has lasted for as many years as it has. However, when one looks at the eruption, there are certain points about it which stand out and which lead me to believe that he is correct in his diagnosis of erythroplasia. These are the duration, the constant expansion of the lesion, the character of the border and the lesion on the penis. I have never encountered a case of erythroplasia like this, but I think that diagnosis is most probably correct.

DR. HOWARD FOX: The part of the eruption in the pubic region looked precisely like Bowen's disease. If that had been the only lesion, there would probably have been a general agreement in the diagnosis. However, the lesion on the penis, as Dr. MacKee suggested, looked like erythroplasia. I do not think this patient has the so-called chronic familial benign pemphigus. There is no familial history of this disease, the lesions existed for years without any remissions and the location is an unusual one. I think the disease should be classed as an unusual type of dyskeratosis, some of the lesions looking like Bowen's disease and some like erythroplasia. The lesion has had nearly every type of treatment except thorough destruction. I strongly suggest electrodesiccation with the patient under general anesthesia.

DR. FRED WISE: I am in agreement with the diagnosis of either Bowen's disease or "bowenoid" disease. In Bowen's original article he describes the disease as epidermoid carcinoma. I favor the treatment mentioned by Dr. Fox. I should attack a small area at a time, anesthetize with procaine hydrochloride and destroy it with the monopolar current.

DR. GEORGE C. ANDREWS: In my discussion at a previous meeting I said that I had had a similar case about five years ago and that in this case the diagnosis in my opinion was erythroplasia and the prognosis was poor. My patient had exactly the same type of eruption clinically on the penis. He was a man about the age of this patient. Six or eight specimens for biopsy were taken from different parts of the lesion. Some were characteristic of erythroplasia, while others showed typical bowenoid epithelioma. This man had treatment along the lines that have been suggested, with destruction by the cutting current.

He also had, as the lesion recurred, a great deal of radium treatment, given by a radium specialist. In spite of that, the disease continued to recur and grew worse. Finally, I began to regret the fact that I had not insisted on complete amputation of the penis when he first came to me. He returned to his home in the South; metastases developed in the inguinal nodes, and he died of squamous cell epithelioma. I think that is the outlook for this man unless radical surgical excision is done. I do not think piecemeal destruction is sufficient.

DR. GEORGE M. MACKEE: I considered all the diagnoses that have been mentioned, as well as others. There has been a pyodermic element in this case, but it is certainly not dermatitis vegetans. I cannot conceive of dermatitis vegetans lasting that long and limited to such a small area and being slowly progressive by a sharp margin, which at times is rolled. The same argument may be used against such diseases as familial benign pemphigus and pemphigus vegetans. I have thought of trying electrocoagulation, but I hesitated because cutting the four biopsy specimens was followed by recurrence in the scars. Two of the speakers mentioned extramammary Paget's disease and Dr. Fraser says he doubts the existence of such a condition. So do I. I think, as he does, that extramammary Paget's disease is Bowen's disease or, sometimes, erythroplasia. I think my patient has erythroplasia, unusual in the distribution and extent of involvement.

Mycosis Fungoides with Bullous Lesions. Presented by DR. FRED WISE.

D. K., a man aged 68, was previously presented before this society on March 25, 1941 as "A Case for Diagnosis (Mycosis Fungoides?) (ARCH. DERMAT. & SYPH. **44**:770 [Oct.] 1941); before the Section of Dermatology and Syphilology of the New York Academy of Medicine on April 1, 1941 as "A Case for Diagnosis (Senear-Usher Syndrome? Mycosis Fungoides?) (ibid. **44**:1121 [Dec.] 1941), and before the Manhattan Dermatologic Society on Oct. 14, 1941 as "A Case for Diagnosis (Mycosis Fungoides?) (not published in Transactions).

Histologic sections from a dry infiltrated lesion and from a bullous lesion examined by Dr. Satenstein and Dr. Sachs "suggested the microscopic picture of mycosis fungoides" Four more histologic sections recently taken, one from a flat superficial lesion, one from a raised nodular plaque and two from bullous lesions, were again examined and studied by Dr. Charles F. Sims. All of these showed the structure suggestive of mycosis fungoides. The description of the bullous lesions was as follows: The epidermis presented moderate acanthosis. In one part of the section there was an intraepidermic bulla, partly filled with fibrin and scattered small, round cells, occasional eosinophils and occasional polymorphonuclear leukocytes. The vessels of the upper part of the cutis were considerably dilated, and the walls were quite edematous and surrounded by a focal cellular infiltration composed of small round cells, occasional wandering connective tissue cells and some larger cells with circular nuclei and with no apparent cytoplasm. Mitoses were not visible. There was a parenchymatous edema of the collagen in the papillary and subpapillary layers. This histologic picture was suggestive of a form of lymphoblastoma.

DISCUSSION

DR. FRED WISE: The reason for presenting this case again is that the diagnosis of mycosis fungoides was not accepted at the previous presentation. The disease was on previous occasions considered to be pemphigus.

DR. HOWARD FOX: The cutaneous lesions looks strikingly like those of mycosis fungoides. The patient now has infiltration in different areas and different degrees of infiltration in the same areas.

DR. J. FRANK FRASER: This case is a typical one of mycosis fungoides with bullous lesions.

DR. EUGENE F. TRAUB: Emphasizing Dr. Wise's reason for presenting this patient again, I recall well that the first time he was shown there was a somewhat general agreement about the diagnosis of pemphigus because of the bullous eruption.

It is interesting to see him some time later, again with the diagnosis of mycosis fungoides, which every one is willing to accept now.

DR. GEORGE M. MACKEE: I have seen this patient a number of times at the clinic, and for a while I hesitated to accept the diagnosis of mycosis fungoides. However, I think now that Dr. Wise has proved his diagnosis, because these plaques are histologically mycosis fungoides and so are the bullae.

DR. A. BENSON CANNON: The lesions in this case are characteristic of mycosis fungoides, but I do not believe that I have ever encountered a case of bullous mycosis fungoides. I should like to know if the specimen removed for biopsy was from a plaque or from normal skin.

DR. FRED WISE: The specimen was taken from a lesion which resembled a varicella vesicle.

Malignant Melanoma. Presented by DR. EUGENE F. TRAUB.

T. P. Z., a boy aged 16 months, was presented on Jan. 27, 1942 (ARCH. DERMAT. & SYPH. **46**:163 [July] 1942).

It is now about two months since presentation, and there has been no change. If anything, some of the pigmented spots in the opinion of the presenter are smaller. One of them seems to be working to the surface. The parents noticed that also. The spots look benign and innocent, and nothing has been done about them so far.

Sporotrichosis. Presented by DR. EUGENE F. TRAUB.

F. B., a boy aged 16, was presented on Feb. 24, 1942 (ARCH. DERMAT. & SYPH. **46**:327 [Aug.] 1942).

The wound on the hand is much improved. It has not healed entirely but has almost done so under roentgen treatment and the use of sulfathiazole dusting powder locally, together with potassium iodide internally. Sixty drops of potassium iodide was given three times a day until about a week ago, when the patient became sick and the dose had to be reduced to 30 drops three times a day. Most of the lumps on the arm have disappeared.

Cultures were definitely positive for sporotrichosis.

MINNESOTA DERMATOLOGICAL SOCIETY

F. W. LYNCH, M.D., *President*

H. A. CUMMING, M.D., *Secretary*

Minneapolis, May 22, 1942

Sarcoidosis. Presented by DR. H. E. MICHELSON, Minneapolis.

A. S., a white woman aged 54, stated that an eruption on her skin appeared in January 1942, on her arms, shoulders and back. When they had once appeared the lesions would never disappear completely, although they changed their appearance somewhat, becoming flatter and pigmented. The patient's nose had been somewhat red for several years, but at the time the cutaneous eruption appeared the nose became darker, inflamed and swollen. She noticed that the swelling and inflammation tended to be worse in the morning. The patient had an eruption on her legs in July 1941, lasting for six weeks. During this period she had a series of small papules on the legs, which increased in size and became bullous. These lesions spread over the lower extremities in the course of six weeks. They disappeared spontaneously, leaving a few pigmented scattered areas. About the middle of March the patient began having a daily elevation of temperature up to 101 F. No loss of weight was noted. She has had no contact with a known tuberculous person since she stopped nursing, about thirty years ago.

Examination reveals a well developed, well nourished white woman whose nose is in striking contrast to the rest of the face because of its dark red color. There is a slight amount of swelling. Scattered over the body, including the breasts and the back, on the arms and on the anterior aspect of the left leg are a few lesions in various stages of development. The involved areas are well circumscribed, and the patches consist of papules which are arranged around the follicles. Some are elevated and some depressed, and there is normal skin between. There is a small amount of scaling on some of the lesions. The older lesions are pitted and brownish. The patches vary from 1 to 5 cm. in diameter. Physical examination otherwise reveals nothing abnormal. Roentgenograms of the lungs and long bones were normal. The Mantoux test gave negative results.

Sarcoidosis. Presented by DR. H. E. MICHELSON, Minneapolis.

A woman aged 50 had nothing in the previous history indicative of the onset of the present illness. A painless tumor developed on the back, the size of which is now 4 by 8 cm. A biopsy established the diagnosis of sarcoid. The Wassermann and Mantoux reactions were negative. Roentgenograms of the chest revealed findings compatible with the diagnosis of sarcoid. From time to time large painless swellings have occurred about the joints and have disappeared. Because of these swellings, roentgenograms were made, but no changes in the bones were discovered. Treatment has been the administering of arsenic, and the lesions have gradually receded. Excision of the tonsils revealed no sarcoid change.

DISCUSSION OF TWO CASES OF SARCOIDOSIS

DR. S. EPSTEIN, Marshfield, Wis.: The first case, in which there were grouped miliary lesions, is one of the most interesting cases I have encountered in a long time. Some of the lesions reminded me of lymphocytomas; however, the microscopic picture showing some tuberculous structure excludes this diagnosis. It is still difficult for me to adjust myself to the enlarging concept of sarcoidosis. I cannot offer a diagnosis because I have never observed a case like this.

DR. HAMILTON MONTGOMERY, Rochester: The grouped follicular lesions on the back suggest lichen scrofulosorum, although the lesions on the face are consistent with lupus pernio or sarcoid. I think this patient's condition exemplifies hematogenous tuberculosis occurring in two different forms and would have been classified by Gans as tuberculosis cutis indurativa. Dermatologists have tended to make too many classifications of tuberculosis; in regard to sarcoid, there is no need of the multiple subdivisions. Histologic changes in the first case are those of sarcoid with epithelioid tubercles. This is also true of lichen scrofulosorum. I believe sarcoidosis occurs in two forms, one in which the lesions are limited to the skin and one in which there is a general systemic sarcoidosis involving the bones, lungs, carotid glands and so forth. In systemic sarcoidosis there may or may not be cutaneous lesions. The cause of sarcoidosis remains to be established.

DR. H. E. MICHELSON, Minneapolis: In the proceedings of the various dermatologic societies one still sees discussion on the difference between sarcoid and sarcoidosis. To my way of thinking, one should not make a diagnosis of sarcoid of the skin but should diagnose the disease sarcoidosis, because I do not believe that the skin alone takes part in this disease; I believe that the other tissues are involved whether the lesions are demonstrable or not.

DR. L. A. BRUNSTING, Rochester: In the first case the patient presents evanescent swelling in addition to the lesions of sarcoidosis. I recall a similar instance in which there was a combination of Darier-Roussy sarcoid and chronic discoid lupus erythematosus. This was some years ago, and treatment was carried out by means of graduated doses of tuberculin. After one particular injection there was a febrile reaction; the patient became sick for a number of weeks but subsequently recovered, and the sarcoid lesions and the swelling disappeared.

Psoriasis. Presented by DR. H. E. MICHELSON, Minneapolis.

O. M., a white woman aged 66, has had an eruption on the legs below the knees since 1932. It has remained almost stationary except for a year's period of complete remission in 1935. There is no seasonal variation. The knees, elbows and skull have never been affected. Various types of therapy have been of no practical avail. Diagnoses of psoriasis, pyoderma and parapsoriasis have been considered at various times.

The lesions are localized in the tibial region and consist of rather bright, erythematous, sharply marginated, noninfiltrated plaques. There is oozing in some areas, and the ordinary silver scales of psoriasis are absent.

DISCUSSION

DR. C. W. LAYMON, Minneapolis: This case has been mystifying for a long time, and it is difficult to make a diagnosis of psoriasis from the lesions which are present today. On one occasion, however, gelatin casts were applied to the legs, and on their removal two weeks later characteristic lesions of psoriasis could be seen. At one time the possibility that the lesions were self induced was considered. The histologic picture fits psoriasis better than any other dermatosis.

Dermatitis Exfoliativa. Presented by DR. JOHN BUTLER, Minneapolis.

N. B., a white man aged 63, has never had any cutaneous lesions to his knowledge until the present attack. In August 1941 a small area of vesicular dermatitis developed on the lower part of his right leg, which was diagnosed as dermatitis venenata (rhus). Despite medication by his local physician (cold packs wet with solution of aluminum acetate N. F.), the eruption extended up the limb, eventually involving the wrists, arms, back, abdomen, face and scalp. The condition became universal three months later. I first saw him on March 16, 1942. His own physician reported that he had been given cutaneous tests at home but that he had reacted to no antigen. Tests of the blood gave negative reactions. Treatment by his local physician consisted of the application of calamine lotion and the tar ointment, which seemed to aggravate the eruption.

Vesiculation has changed to a scaly erythema. There is mild itching, and the integument is deep red. The skin is thickened and covered with large wide, quadrilateral scales, attached at one edge. Desquamation is profuse, and every morning the patent's bed contains a large quantity of scales. Beneath the scales the dusky red skin is somewhat smooth and dry. There is considerable itching at times, and moist lesions appear now and then on the lower parts of the legs. Much of the hair on the scalp has fallen out. This condition has improved at times, but fresh exacerbations occur.

Physical examination reveals no abnormalities and eliminates the possibility of a focal infection. The patient complains of chills, at times slight and at times severe. His appetite is good, he feels well and his temperature has at no time been higher than 99 F. Dry treatment has been tried and seems unsatisfactory. Starch and soda baths three times a day are comforting. Phenolized zinc oil (phenol 2.4 Gm., zinc oxide 144 Gm. and olive oil, to make 240 cc.) applied during the night controls the itching fairly well. He is taking vitamin B complex and vitamin A, 25,000 U. S. P. units daily. Because of the infiltration of the face an ectropion developed, with subconjunctival hemorrhage of the right eye. He has had two or three mild recurrences since I saw him in March. He sleeps poorly at times. The infiltration of the skin has lessened considerably.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I believe that there are few cases of primary exfoliating dermatitis. Most of the patients have exfoliations secondary to some other disease.

DR. L. A. BRUNSTING, Rochester: The first consideration in the differential diagnosis deals with the possibility of lymphoblastoma. Sometimes all sources of

information in the general examination fail to present confirmatory findings, even the biopsy of the skin or of the lymph nodes, and a course of expectant treatment is needed in order to settle the matter. It is often difficult to distinguish between disseminate neurodermatitis and psoriasis, especially when the processes are universal.

DR. HAMILTON MONTGOMERY, Rochester: I did not think this case was one of exfoliative psoriasis. I failed to see changes in the nails typical of psoriasis. The histologic picture showed severe intracellular edema and spongiosis, as one would see in contact dermatitis, but this, of course, could be secondary to treatment with stimulating applications. In some cases psoriasis starts as exfoliative dermatitis. The histologic picture of psoriasis remains as such even in its exfoliative stage.

Erythema Annulare Centrifugum. Presented by DR. H. E. MICHELSON, Minneapolis.

A white woman aged 47 has had lesions on her right forearm for the past four years, which consist of nodules arranged in a serpiginous manner without ulceration. Several Wassermann reactions were negative. Twenty injections of a bismuth compound were administered without causing any appreciable change in the lesions.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: There are various forms of this disease, and of course very little is known about it.

Epidermolysis Bullosa Acquisita. Presented by DR. H. E. MICHELSON, Minneapolis.

This man, aged 48, is a mechanic. He states that for the past ten years any injury to his hand has resulted in the formation of blisters. When he was seen in November 1940 by Dr. Rusten he had a number of blisters on his hands, which responded to mild treatment.

At this time he was seen for blisters following applications to the leg. An examination of the site of the previous lesions disclosed milium-like scarring and atrophy of the skin of the fingers.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: It is important for one to realize that a patient with epidermolysis bullosa may become a great problem when occupied in a manner which produces trauma of the hands. In this particular case compensation was the issue.

DR. L. A. BRUNSTING, Rochester: The distribution of the lesions and their occurrence during the heat of summer brings up the probability of photosensitivity. There are few scars from previous lesions. It may be well to check the urine for abnormal amounts of porphyrins and to test the reaction of the skin to various forms of radiation to see what reaction can be provoked.

Mixed Tumor of the Skin. Presented by DR. S. E. SWEITZER, Minneapolis.

H. M., a white man aged 83, first noted a small papule on the left eyebrow about one year ago. The lesion was painless and grew steadily in size. During the past two months the growth has been rapid. There were no cutaneous tumors elsewhere. Examination shows only the postoperative scar just above the medial portion of the left eyebrow.

DISCUSSION

DR. H. MONTGOMERY, Rochester: At first glance the lesion suggested naevus epitheliomatocylindromatosus, but in addition there are glandlike structures associated with a bluish-staining mucin-like substance, which, I believe, would prove with special stains to be mucin. I agree with the diagnosis of mixed tumor of some sort.

Nevus. Presented by DR. C. W. LAYMON, Minneapolis.

J. S., a white boy aged 10 years, has an eruption on the left side of the neck and arm which developed about Jan. 1, 1942. There had been no previous abnormalities of the skin.

Examination reveals a telangiectatic pigmented, somewhat linear lesion extending from the left side of the neck down the left arm.

DISCUSSION

DR. C. W. LAYMON, Minneapolis: I thought that this eruption was a nevus, but was undecided as to the type. There was some difference of opinion among those who examined the patient as to whether it was a naevus pigmentosus or one of the telangiectatic type. I should like to hear what Dr. Montgomery has to say about the histologic findings.

DR. H. MONTGOMERY, Rochester: I could not be sure of identifying any nevus cells in the section. The lesions seemed to be of an inflammatory nature rather than a true nevus. Clinically the lesions did not fit in with lichen striatus.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. S. E. SWEITZER, Minneapolis.

V. D., a white woman aged 20, first noted pea-sized lesions on the right ankle four years ago. There was considerable purulent drainage from them two years ago. The lesions on the right arm and on the left arm appeared three years ago and one year ago respectively. All lesions have since slowly increased in size.

Examination shows low plaques on the aforementioned areas which are pink centrally and light brown at the borders with yellowish white scales. Telangiectasia is also noted in the lesion on the right arm.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I have no explanation as to why such cases were not encountered in previous years. Certainly they must have existed.

DR. S. EPSTEIN, Marshfield, Wis.: I may be able to answer to some extent the question of why cases of necrobiosis were not observed prior to Oppenheim's and Urbach's description. At the University Dermatologic Clinic in Breslau, I encountered 2 cases of this disease. The first was presented in 1925. At various times the diagnosis of granuloma annulare, scleroderma and atypical tuberculid was made. The histologic picture was typical of necrobiosis.

Weed Dermatitis. Presented by DR. H. E. MICHELSON, Minneapolis.

A. D., a white man aged 30, complained of an eruption on the forehead, between the fingers, on the forearms, above the ankles and on the back of his knees, which began seven years ago. It increased in severity from August to October of every year. The itching was intense. There was no family history of any allergic disease obtainable.

This patient presents a maculopapular eruption on the forehead, face and upper lip and between the fingers. Patch tests with plants of the ragweed group elicited 4 plus reactions.

DISCUSSION

DR. L. A. BRUNSTING, Rochester: There has been a great deal of discussion lately about the technic of desensitization of patients with contact dermatitis, especially in the field of poison ivy and weeds. I have never observed any consistent variation in the reactions to patch tests of patients who have been subjected to the oral or injection method of desensitization, although in some instances there is a break in the cycle of recurrent episodes of eruption.

Book Reviews

Surgery of the Ambulatory Patient. By L. Kraeer Ferguson, M.D., F.A.C.S., Assistant Professor of Surgery, University of Pennsylvania. Section on Fractures by Louis Kaplan, M.D., F.A.C.S., Associate in Surgery, University of Pennsylvania. Price, $10. Pp. 900, with 645 illustrations. Philadelphia: J. B. Lippincott Company, 1942.

The subject covered in this new book is one which the author thinks has been much neglected in the modern practice of medicine. The lesions which he discusses are those which are seen in office or dispensary practice and which can be treated when the patient is ambulatory. No procedure is described which has not been actually carried out on ambulatory patients.

As the subject of the book is so diversified, the author has obtained the help of numerous colleagues in its preparation. Dr. Donald M. Pillsbury has made contributions and suggestions for the dermatologic portions.

The good common sense of the author, which is constantly evident, is shown in discussing the care that must be exercised in doubtful cases. "Smallness," he states, "is not at all synonymous with unimportance." He adds that the general practitioner who usually recognizes acute appendicitis will often fail to recognize or appreciate the danger of a small malignant growth or a boil on the upper lip.

The book is divided into three parts: Part 1, Surgical Principles and Lesions; Part 2, Regional Surgery, and Part 3, The Musculoskeletal System, confined mostly to fractures and dislocations. The first two parts of the book, consisting of more than three fourths of the text, contain the subjects of interest to the dermatologist.

Part 1 is divided into twelve sections and contains descriptions of the causes, symptoms and treatment of many lesions of different types. There is an excellent discussion of the various methods and drugs used for producing anesthesia. The author condemns the use of ethyl chloride as a local anesthetic for any cutting operation. However, he does not mention its value as a quick anesthetic for the use of the bone curet in removing lesions like seborrheic keratoses and common warts. In fact, the use of the sharp curet is apparently not mentioned in the book.

The preparation of the patient for operation, postoperative care and useful dressings and bandages are discussed. The dressings and bandages are illustrated by excellent drawings and photographs which are easily understood. A full description is given of the Unna gelatin "boot" for the treatment of varicose ulcers and other diseases. The author considers this "the most serviceable supporting dressing" and prefers it to the prepared gelatin bandages. He also gives some valuable practical suggestions for the application of the boot.

In discussing furuncles, he calls attention to the "dangerous area," chiefly the upper lip and nose, as these parts are in constant motion, which hinders the localization of the infection. He warns of the possibility of progressive thrombophlebitis and of thrombosis of the cavernous sinus, which though rare is usually fatal.

All moles which are subject to constant trauma, the author thinks, should be removed. He calls attention to the potential danger of the blue-black mole, especially on the feet, as in this location are seen 50 per cent of the lesions which eventuate in malignant melanomas.

Other lesions described in Part 1 include inflammations due to infection, open wounds, burns, foreign bodies, cysts and tumors. The section discussing furuncles, abscesses, erysipelas, dermatitis repens, chronic burrowing ulcers and insect and human bites should be of special interest to the dermatologist.

The book is profusely illustrated with excellent photographs and drawings of diseases, operative procedures, apparatus, dressings, etc. A few of the photographs showing results of treatment, as on pages 260 and 261, are unsatisfactory. The

bibliography is adequate, and the printing and general appearance of the book are all that could be desired.

While the book has been written mainly to aid the general practitioner and the younger surgeon, it contains a wealth of valuable material for the dermatologist, including discussions of general surgical principles and individual operative procedures. It is highly recommended for every dermatologist.

El mal del pinto, pinta o carate. Su historia, su etiologia, su patogenia. By Francisco Leon y Blanco, M.D. Pp. 227, with 27 illustrations. México, D. F.: Compania General Editora, S. A., 1942.

Now that large armies are being sent to distant parts of the world the knowledge of tropical diseases is becoming of paramount importance. Mal del pinto (pinta or carate) is a disease which is practically unknown to the majority of American physicians. Its importance, nevertheless, is evident, judging by the number of patients affected. The author estimates that probably 1,000,000 cases exist at present in Latin America, of which 270,685 are in Mexico and about 400,000 in Colombia.

Dr. Leon y Blanco is well known because of his original contributions on this subject. He started a new conception of pinta by his studies on its early manifestations and by showing that the late pigmentary changes are not the only ones which occur.

This excellent study of pinta is divided into eight chapters covering the geographic distribution, history, evolution, etiology, serology, diagnosis, prognosis and treatment. A bibliography of two hundred and eleven references is also included.

In a study of the geographic distribution, it is interesting to note that in Cuba, where many valuable contributions have been made, including the discovery of the causative spirochete, the number of cases is less than 200. The chapter on the history of pinta is interesting and abounds in references. The epidemiology, entirely reviewed in the light of the new concept of the disease, shows that pinta usually starts in persons between 10 and 20 years of age. The most interesting chapters are those which relate the early manifestations (the initial lesion and the "pintids"), which were first described by the author. Their different types are carefully discussed from both clinical and histologic standpoints. Immunologic problems of the disease are also thoroughly considered.

This monograph will be a useful reference book to those interested in tropical diseases in general and in pinta in particular. The book is of pocket size with paper cover.

Directory of Medical Specialists. Compiled by the Advisory Board for Medical Specialties. Second edition. Price, $7.00, cloth. Pp. xvi plus 2,495. New York, Columbia University Press, 1942.

The publication of the second edition of the Directory of Medical Specialists should be welcomed by a host of physicians who have found the first edition invaluable. A book of this character represents an immense amount of work and reflects the greatest credit on the editor and his staff.

This edition contains four thousand more names than the first one and gives information about more than eighteen thousand specialists certified by the various American specialty boards. It also gives more complete information about each certified specialist.

A separate section is devoted to each of the fifteen major boards, in which the biographic data are listed geographically according to state and city. There is also a general alphabetical index of names and addresses of all certified specialists.

The directory continues to be of great value to both general practitioners and specialists and to hospitals, libraries and medical societies. It has also been found of great value to the government in giving reliable information about physicians in the armed forces. The work of the Columbia University Press is all that could be desired.

Modern Treatment of Venereal Diseases. By E. T. Burke, D.S.O., M.B., Ch.B. (Glas.); Lieutenant Colonel (late) Royal Army Medical Corps; formerly Director of the London County Council (Whitechaple) Clinic; Consultant Venereologist in the Public Health Department of the London County Council; Lecturer in Venereal Diseases in the London Hospital Medical College, University of London. Pp. 90. London: John Bale & Staples, Ltd., 1942.

This little book is the result of many years of experience of a man who up to the time of his recent death was one of England's outstanding authorities on venereal diseases. As is inevitable in so brief a treatise the author is inclined to be dogmatic. When founded on his own experience, his preferences in treatment are the result of authoritative critical analysis. Unfortunately, however, he has included suggested treatments for lymphogranuloma venereum and the care of arsenical drug reactions, such as "hemorrhagic encephalitis," which are obviously the result of hearsay rather than experience. Apart from such minor exceptions, the author has condensed within a brief space a great deal of carefully sifted information.

In general, his principles of treating syphilis are in accord with those of the Cooperative Clinic Group in the United States. He favors continuous rather than intermittent alternating courses of arsenical and bismuth drugs. He rejects concurrent therapy with both types of drugs because of the increased danger of toxic reactions and because of his experience that this scheme of treatment predisposes to reagin fastness. Plans of therapy of the various stages and types of syphilis are given which can be of great aid to the general practitioner.

The author's outstanding contribution to the treatment of early syphilis is his insistence on computing the efficacy of treatment on the basis of the two factors, time and quantity of drug. Using these two factors, he has evolved a somewhat complicated but valuable scheme of computing an efficiency index. He claims that an efficiency index of over 60 will insure cure in practically 100 per cent of cases when treatment of syphilis has been started in the acute stages. From a scientific point of view one can quibble over Burke's admittedly somewhat arbitrary assignment of therapeutic values to certain quantities of drugs, but there can be no question that his efficiency index can be a valuable aid in determining the adequacy of routine treatment for early syphilis. In clinic practice, however, the usual problem is determining not the adequacy of ideal treatment but how to make patients return regularly for a period of fifty weeks or over in order to obtain an efficiency index of over 60. It is doubtful if Burke's formula for computing this index can be of much value in the new experiments with attempted quick cures of early syphilis, although the principles underlying his concept are sound.

In the section dealing with the treatment of gonorrhea the great value of sulfonamide compounds is accepted, but the use of the various preparations coming under this heading changes so rapidly that no textbook at the moment can claim to give the most modern or best form of therapy. The value of fever therapy in stubborn cases of gonorrhea is suggested but not stressed.

Occupational Tumors and Allied Diseases. By W. C. Hueper, M.D. Price, $8. Pp. 896. Springfield, Ill.: Charles C Thomas, Publisher, 1942.

An astonishing amount of valuable information for the dermatologist is contained in this impressive book of reference. Of 720 pages dealing with occupational tumors of all organs and tissues, 280 pages, or nearly 40 per cent, are devoted to tumors of the skin. The author has carefully analyzed evidence obtained from innumerable sources and has attempted to "correlate and evaluate the various observations made, and theoretical conceptions advanced so as to form a well balanced and when possible, coherent picture of the subject under discussion." He has done this in a masterly way and shown his knowledge of pathology, chemistry and details of manufacturing processes.

The book is written for the benefit of the medical profession, governmental agencies in charge of public health supervision of working conditions and sanitary

control of various types of merchandise, legislative bodies, workmen's compensation boards, lawyers, industrial engineers, life insurance companies and research workers in biology, chemistry and physics. Such a large list of professions shows the wide scope of the volume.

The chapter of special dermatologic interest is entitled "Occupational and Accidental Tumors of the Skin and Its Appendages." A general division is made of the effects of (1) chemical and (2) physical agents. Among the inorganic chemicals, special attention is given to arsenic, while the organic chemicals include, among others, (*a*) coal, asphalt and mineral oils, (*b*) pitch and tar, (*c*) distillate products of mineral oils, (*d*) creosote, (*e*) anthracene, (f) soot, (*g*) aromatic hydrocarbons, coal tar dyes, etc., and (*h*) substances producing chemical traumatic cancer. Physical agents producing occupational tumors include actinic agents (ultraviolet and roentgen rays) and various types of trauma-producing agents. As tumors of the skin are so often preceded by dermatoses, the author has devoted considerable space to a discussion of this subject. This constitutes an additional feature of great interest to the dermatologist. It might be added that the author has described the cutaneous changes in excellent language.

In the discussion of the more important subjects, sections on historical and technologic aspects are given, followed by descriptions of such items as geographic incidence, symptoms, location and multiplicity of lesions, age, sex, duration of exposure, histologic changes and animal experimentation. Any one of the more important subjects, such as tumors due to arsenic, tar, oils or actinic agents, would make the book worth having. In discussing arsenic, the author cites fifty-five occupations in which the workers are exposed to arsenical preparations. He adds that there are numerous additional occupations which provide regular contact with arsenical preparations and represent sources of arsenical dermatosis and cancer.

The book contains a chapter on special aspects of occupational tumors, including age, span of life, sex incidence and organ and tissue specificity. The various theories of the causation of cancer and their relation to occupational neoplasms are then discussed. The final chapter deals with the medicolegal and public health aspects of the subject.

An extensive bibliography is included and helps to make the book a valuable one for reference.

The book is clearly and carefully written and should be indispensable to all physicians who are interested in cancer and other neoplasms of occupational origin. It should also be of great interest and value to every dermatologist.

News and Comment

DIRECTORY OF DERMATOLOGIC SOCIETIES

Frequent complaints have been made about inaccuracies in the "Directory of Dermatologic Societies," which is published several times a year in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. The difficulty in getting up-to-date accurate information is due to failure of the secretaries of the respective societies to inform the editor of changes in the personnel of their officers. It is earnestly requested that all secretaries of dermatologic societies supply the desired information as soon as possible after the election (usually annual) of their officers.

DEATHS

Dr. Edward R. Maloney, 136 East Sixty-Fourth Street, New York, died. Oct. 5, 1942.

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